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Little (Arthur D.), Inc., Cambridge, MA

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This report describes an integrated exposure and risk methodology developed for the U.S. Environmental Protection Agency (EPA) as part of a program to assess exposure/risk of 65 classes of chemicals (129 "priority pollutants") in the water environment. It provides an overview of the risk assessment process and a detailed discussion of the analytic components of an environmental exposure and risk assessment including approaches for evaluating:

- the environmental loadings resulting from production, transport, use, and disposal of the chemicals;
- the mechanisms of pollutant transport and transformation in environmental media and the concentrations detected;
- the extent of exposure of humans and other biota; and
- the risk presented to exposed populations.

The methodology is intended to provide a general understanding of environmental exposure and risk assessment and to assist those who will be conducting this type of analysis. It contains numerous examples from exposure and risk assessments of 54 priority pollutants performed for EPA and a bibliography of source materials.

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AN APPROACH TO ASSESSING EXPOSURE TO AND RISK OF ENVIRONMENTAL POLLUTANTS

by

Arthur D. Little, Inc.

Michael Slimak
Project Manager
U.S. Environmental Protection Agency

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Monitoring and Data Support Division (WH-553)
Office of Water Regulations and Standards
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OFFICE OF WATER REGULATIONS AND STANDARDS
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U.S. ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

FOREWORD

Effective regulatory action for toxic pollutants requires an understanding of the ecosystem and human health risks associated with the manufacture, use, and disposal of the substance. The process of assessing these risks needs to develop information on the fluxes of the substance through the technosphere and through the biosphere, and to couple this with information on its biological effects. The analysis is thus intended to allow an informed judgment about the likelihood of environmental harm and to provide insight into the potential effectiveness of alternative actions to control or reduce any unacceptable risks.

This document describes the exposure/risk assessment methodology developed as part of a program to address 65 classes of chemicals (or 129 individual "priority pollutants") named in the 1977 Clean Water Act. The methodology is multi-media in scope, enabling all facets of environmental risk to be viewed in perspective.

The methodology begins by identifying releases to the environment during production, use, or disposal of the substance. It proceeds with evaluating the fate of the substance in the environment and the resulting ambient levels. It then predicts the human and aquatic life exposure to the substance and, after interpreting the available data on toxicity, provides an assessment of risks.

The methodology has been applied to the nationwide assessment of several dozen of the priority pollutants, and numerous examples taken from this work have been presented. The analytical elements, however, have been found to apply readily to local, as well as nationwide studies.

Michael W. Slimak, Chief
Exposure Assessment Section
Monitoring & Data Support Division (WH-553)
Office of Water Regulations and Standards

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1.0 TECHNICAL SUMMARY

There is a continuing need on the part of regulatory agencies and private industry to describe and interpret the impacts of potentially toxic substances in the nation's environment. In this context, exposure and risk assessment methods are required to permit a quantitative characterization of the sources, environmental pathways, and human or environmental effects of specific substances. In order to assist in the determination of appropriate regulatory actions, the Monitoring and Data Support Division (MDSD) of the Office of Water Regulations and Standards (OWRS), U.S. Environmental Protection Agency (U.S. EPA) has developed an integrated, systematic approach for performing exposure and risk assessments, and has applied this approach to approximately sixty environmental pollutants of concern. Although the approach was developed using waterborne pollutants, its elements may be applied in a wide variety of situations at varying levels of detail. This report describes the exposure and risk assessment methodology and provides selected examples of the use of the methodology.

For purposes of this report, exposure is defined as the encounter of a substance in the environment by human or animal populations, and risk is defined as the probability of an exposed organism suffering an adverse effect as the result of such exposure.

The scope of an exposure or risk assessment may be characterized by a number of key features:

- Geographic scale, which may be global, national, regional, or local.
- Pollutant sources, which may include industrial, residential, commercial, and non-point sources.
- Environmental media, which may include air, surface water, soil, groundwater, biota, or any combination thereof.
- Pollutants addressed, which may be a specific substance or a class of related substances.
- Receptor populations considered, which may include humans, animals, plants, micro-organisms, or specific sub-populations of the above that are exposed to unusually high pollutant levels.
- Adverse effects considered, which may include acute or chronic health effects as well as environmental effects.

- Time frame of the assessment, which may be retrospective, current or prospective.

- Intended use of the assessment, which may be for regulatory, scientific, or public information purposes.

The methodology summarized and described in this report is sufficiently flexible so that it can be applied with respect to any of the above definitions of scope.

An environmental exposure and risk assessment for a chemical substance generally consists of a series of analytic components, or modules, each addressing a particular set of relevant information about the substance. These components are linked together as shown in Figure 1-1, culminating in an evaluation of risks to humans and other biota due to the presence of the substance in the environment. The essential aspects of each component are as follows:

- Initial Considerations--the available information about the substance and important environmental issues are identified, the scope and focus of the detailed exposure and risk assessment are established, and the subsequent work effort is planned and organized.

- Materials Balance--the significant pollutant sources are identified, and the locations and magnitudes of environmental releases are characterized. This involves a systematic examination of the various activities which produce, transport, use, or consume the substance, and often requires estimation of environmental loadings in the absence of empirical knowledge.

- Monitoring Data--the concentrations of the pollutant in all environmental media are investigated through scanning of field data, and important temporal or geographic variations are noted. The monitoring data provide a means of confirming some of the materials balance and environmental fate estimates.

- Environmental Pathways and Distribution--the mechanism of pollutant transport and transformation in the environment are investigated, leading to an assessment of the substance's persistence and its likely partitioning among the various environmental compartments. This may involve the use of mathematical models to estimate the distribution of the substance in specific media.

- Exposure of Humans and Other Biota--the potential exposure of humans and other species is assessed through an investigation of the important environmental exposure routes and the extent or frequency of exposure. For

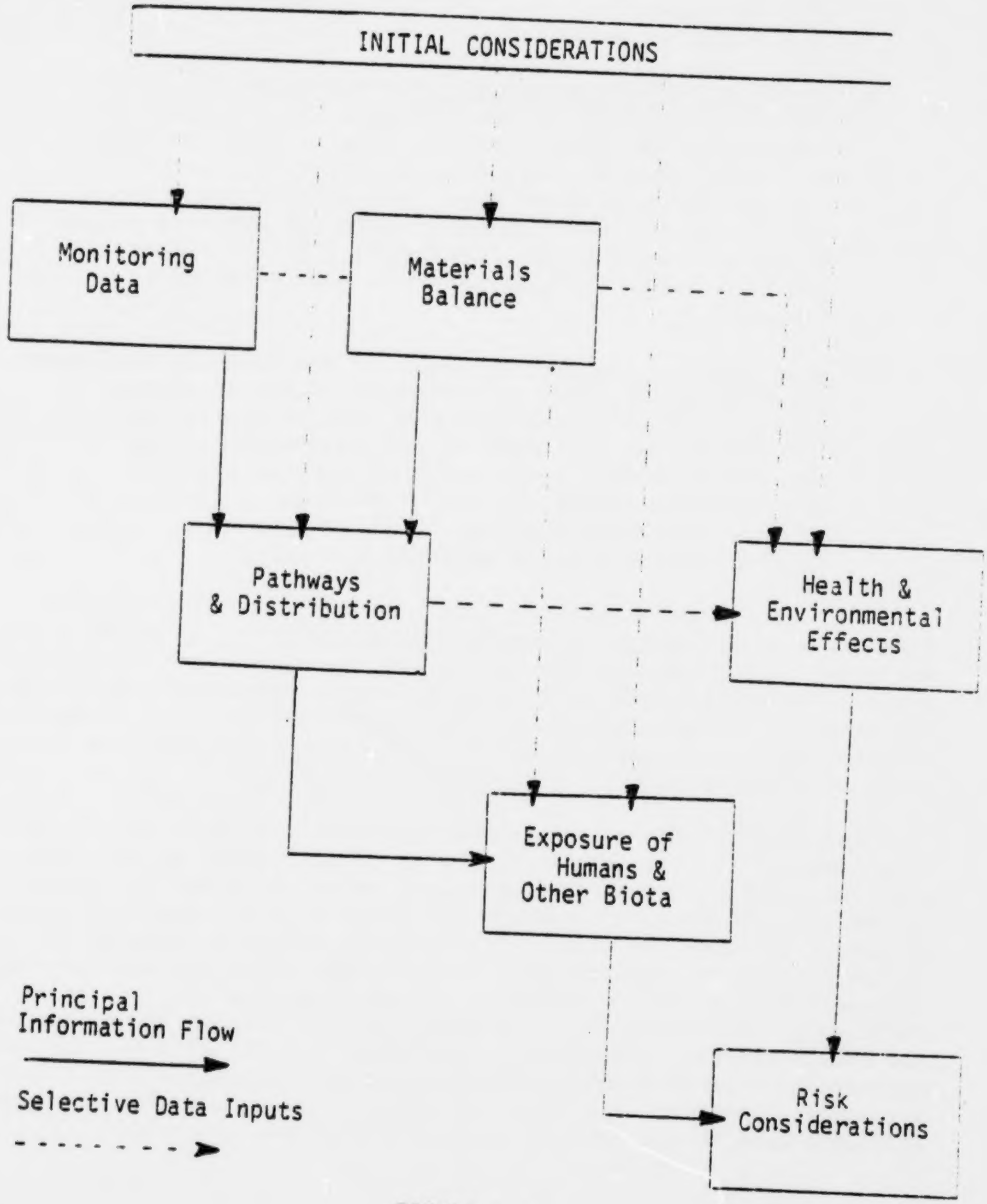
INITIAL CONSIDERATIONS
Monitoring Data
Materials Balance
Pathways & Distribution
Health & Environmental Effects
Exposure of Humans & Other Biota
Risk Considerations
Principal Information Flow
Selective Data Inputs

FIGURE 1-1

MAJOR COMPONENTS IN ENVIRONMENTAL EXPOSURE AND RISK ASSESSMENT humans this may address not only geographic differences, but also the identification of specific subpopulations that may have higher than average exposure via ingestion, inhalation, or dermal absorption.

- Health and Environmental Effects--the potential acute and chronic effects of the substance are evaluated for both humans and other species. Data on human effects may come from either epidemiological or laboratory studies, and will focus upon those effects most pertinent to the prevalent chemical forms and exposure routes of the substance in the environment. To the extent possible, metabolic information is also taken into account.

- Risk Considerations--the results of the previous components are combined to yield an assessment of the potential health risks to humans and other species due to the presence of the substance in the environment. This may involve simple comparisons of toxic levels with environmental levels, or, as in the case of carcinogenic effects, may require extrapolation of laboratory animal dose-reponse data using mathematical models.

Each of the above components is treated in detail in separate chapters of this report. A comprehensive discussion is given of the means for collecting and interpreting relevant data, formulating and applying analytic models or techniques and consolidating and presenting the results. In addition, specific examples are provided of how these methodological components have been used for exposure and risk assessments of selected priority pollutants.

An important issue that is addressed throughout the report is data adequacy and the associated levels of confidence in the exposure and risk assessment results. Depending on the accuracy and completeness of the required data, the results can range from well-defined numerical estimates to rough qualitative statements. Moreover, many of the techniques utilized to analyze data, notably fate modelling and dose-response extrapolation, involve a number of assumptions which may not be fully verifiable. Therefore, it is crucial that the outputs of the exposure and risk assessment are properly qualified in terms of model and data limitations. Despite such limitations, a well-organized and scientifically-documented assessment can be an extremely useful instrument for understanding pollutant impacts and guiding regulatory actions.

2.0 INTRODUCTION

2.1 BACKGROUND

The growing concern regarding the nature, distribution, and potential effects of toxic and other hazardous chemicals in the nation's environment has been reflected in many federal government statutes, regulations, and rules. The Clean Water Act, the Clean Air Act, Resource Conservation and Recovery Act, Toxic Substances Control Act, and regulations under these statutes have addressed these concerns, and several regulatory agencies are charged with implementation of environmental management responsibilities (for example, the Environmental Protection Agency, Consumer Product Safety Commission, and the Food and Drug Administration). Industry organizations and independent research groups have also investigated sources, pathways, and effects of potentially toxic materials and the exposure for humans and other species to these materials as part of a nationwide environmental program.

Throughout many of these efforts, there has been a focus on the analysis of risks associated with the presence of toxic and hazardous chemicals in the environment. This analysis process, often referred to as "risk assessment" or "exposure assessment," encompasses many aspects including in-depth toxicological experimental investigations of health effects using laboratory animals, environmental monitoring and measurements, and extensive data collection and/or modeling efforts to determine and predict the concentrations and fate of toxic substances in the environment. This work is expected to continue at many levels, both publicly and privately sponsored, throughout the foreseeable future.

The Monitoring and Data Support Division (MDSD) of the Office of Water Regulations and Standards (OWRS), U.S. Environmental Protection Agency (U.S. EPA), is conducting a program to evaluate the exposure to and risk of pollutants in the nation's environment. Part of this effort is a result of the settlement agreement between the Natural Resources Defense Council (NRDC) and the Environmental Protection Agency (U.S. District Court, D.C., 1976)[1]. Under this agreement, the Monitoring and Data Support Division is evaluating the exposure and risks to human and non-human species resulting from the occurrence of 129 specific chemicals in the water environment (hereafter referred to as the 129 priority pollutants). On the basis of these evaluations, recommendations for regulatory actions are prepared to reduce the exposure to and risks of priority pollutants in the environment. In order to provide a systematic and comprehensive evaluation approach, an integrated risk assessment methodology is being developed. This methodology is the subject of the report.

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[1] U.S. District Court, District of Columbia. Settlement Agreement between National Resources Defense Council, Inc. (Civil Action Nos 2153-73 and 75-1267), Environmental Defense Fund (Civil Action No 75-0172), Citizens for a Better Environment (Civil Action No 75-1698) et al. and Russell E. Train and James I. Agee et al.; June 7, 1976.

2.2 TYPES OF EXPOSURE AND RISK ASSESSMENTS

Exposure and risk assessments vary with respect to their scope and use. The scope of the assessment can be described by several parameters. The scale of an assessment is defined by whether global or national, regional or local exposure or risks are considered. An assessment can also be characterized by which populations are considered (humans, plants, animals, microorganisms, or all environmental species) and whether average nationwide risks are evaluated or risks to specific subpopulations in specific areas. The time frame of an assessment can be retrospective, current, or prospective. Finally, an assessment can include evaluation of one or many of the potential health or environmental effects associated with the presence of a toxic substance in the environment.

An exposure assessment involves examination of all factors that lead to an exposure for human and other species to the pollutant and a quantification of that exposure. A risk assessment includes all the elements of an exposure assessment and a qualitative or quantitative estimation of the risk to a given population based upon the exposure to and effects of a pollutant (e.g., the increased risk of carcinogenicity to the total U.S. population associated with the environmental presence of a chemical). Throughout this report we will use the terms "risk assessment" and "exposure assessment" interchangeably, recognizing that risk assessments combine both analysis of exposure and analysis of effects to yield an assessment of risk. (In the published literature, these quantitative relationships between risk and exposure are often called risk assessments.)

Risk assessments may have many different uses. Typical uses include: development of regulatory approaches, requirements, or recommendations; development of environmental standards and/or criteria; establishment of information, monitoring, or research needs; providing public information, education, etc. Table 2-1 characterizes risk assessments in accordance with all of these general parameters. The methodology described herein is called an integrated risk assessment methodology since, in principle, the approaches used are applicable to all types of risk and exposure assessment, independent of scope, depth or other characteristics: specific portions of the methodology are suitable for independent studies and assessments.

2.3 REPORT OBJECTIVES AND CONTENT

The objective of this report is to describe an integrated exposure and risk assessment methodology. The methodology is intended to be used by public and private organizations and individuals who seek guidance on

TABLE 2-1. PARAMETERS THAT CHARACTERIZE RISK ASSESSMENTS

Scale	-	National, regional, local
Populations Considered	-	Humans, plants, animals, microorganisms, all species
Time Frame	-	Retrospective, current, prospective
Potential Effects	-	Human Health--carcinogenicity, chronic functional disorders, etc.
	-	Ecological--habitat, foodchain, reproductive, etc.
Intended Use	-	Development of regulations, environmental standards, criteria
	-	Establishment of information or research needs
	-	Public information/education

conducting exposure and risk assessments, and to provide a foundation for further development of the methodology. Not all portions of the methodology have been considered in the same depth of detail. For certain aspects of the analysis, such as ecological modeling and toxicological research, unique methodological approaches have already been developed to a high degree of sophistication. Therefore, users may require additional detail in some areas depending upon the overall purpose, level of effort, and intended use of the individual risk assessment. This report presents basic approaches to risk assessment so that users may select the most appropriate segments for each specific application. The general approach is intended to guide the planning and conduct of specific exposure or risk analyses rather than provide a detailed procedure. Since this risk assessment methodology was developed for the EPA to address waterborne priority pollutants, it is focused on assessment of exposure and risk where water contamination or pollution is significant.

Chapter 3 of this report provides an overview of the risk assessment process, including the goals and objectives of each major component, the flow of information from one analysis area to another, and some of the major assumptions and limitations of the process. The initial steps of a risk or exposure assessment are then discussed. In Chapters 4 through 9, approaches to each component of the risk assessment process are described in some detail. The organization of these chapters is as follows:

Chapter 4--Materials Balance--Source Identification and Loading Estimation

Chapter 5--Environmental Pathways and Fate Analysis

Chapter 6--Monitoring Data and Environmental Distribution

Chapter 7--Human Exposure and Effects

Chapter 8--Exposure and Effects--Non-Human Biota

Chapter 9--Risk Considerations

In each of these chapters, examples are drawn from actual exposure and risk assessments performed for EPA. These examples are intended to illustrate methods of data analysis or presentation and the reader is referred to the full report for specific information regarding each pollutant.

Chapter 10 provides a bibliography of source materials for the conduct of exposure and risk assessment of environmental pollutants. This bibliography is intended to give the investigator an initial means of obtaining the numerous types of information needed to assess exposure and risk.

The appendix discusses some of the mathematical details of quantifying risk.

3.0 EXPOSURE AND RISK ASSESSMENTS--AN OVERVIEW

3.1 OVERVIEW

The general goals of an environmental risk or exposure assessment are shown in Table 3-1. Only some of these goals may actually be realized in a specific risk assessment, depending upon the specific pollutant, the resources available, and the time allowed for the assessment process.

Figure 3-1 shows the major components of the risk assessment process. The initial considerations component is intended to establish the scope and focus of the risk assessment, assign priorities for investigation of specific environmental pathways, exposures or effects, and provide the initial basis upon which to proceed with the risk assessment. The materials balance component refers to a description and quantification of the flow of a pollutant from its generation through its initial release into the environment. The environmental pathways and distribution component refers to analysis of the pathways traversed by the pollutant in the environment, the intermedia and intramedia transfers that occur, and the resultant environmental distribution, both spatial and temporal. Monitoring data can provide a major input into the establishment of the pollutant distribution. The exposure assessment component attempts to characterize the type, size, location, and distribution of populations and subpopulations--human and other biota--exposed to a pollutant in the environment and to establish actual and potential exposures to the pollutant in terms of extent, duration, level, etc. The health and environmental effects component analyzes the known or anticipated acute, chronic, and other effects of pollutants on humans and other species. If possible, it provides a basis for extrapolation of the results of laboratory effects studies to real environmental situations and/or extrapolation of results of studies with laboratory animals to human population groups. The risk considerations component summarizes previously developed information, estimates quantitatively, if possible, the risks to various population groups, and places the risks associated with pollutants, sources, environmental pathways, exposure routes, and health effects in perspective.

As shown in Figure 3-1, the major flow of information is from materials balance and monitoring data components to environmental pathways and distribution components. These data, combined with environmental fate analyses, lead to analysis of exposure of humans and other biota. Exposure and health effects analyses are combined to yield risk estimates. Materials balance has indirect inputs to health and environmental effects and exposure components; similarly, environmental pathways and distribution analysis have indirect inputs to health and environmental effects.

In the remainder of this chapter, each of the major components in the risk assessment process is discussed briefly, including focusing on the goals and objectives of these steps, some of the approaches used, and

TABLE 3-1. GENERAL GOALS OF ENVIRONMENTAL RISK ASSESSMENT

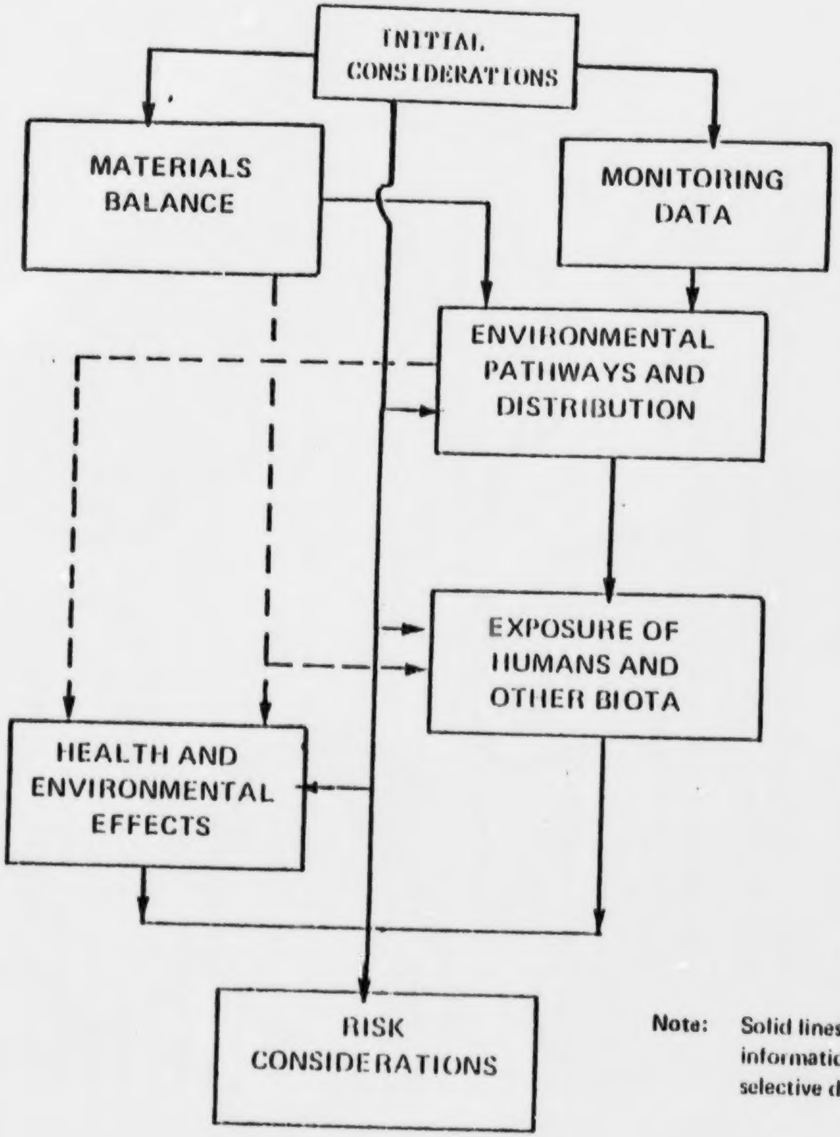
Establish pollutant sources, pathways and distribution

Establish exposure to and effects of pollutants

Quantify the human health and biotic risks

Provide information base to derive approaches to risk reduction

Identify data gaps and research needs


INITIAL CONSIDERATIONS
MATERIALS BALANCE
MONITORING DATA
ENVIRONMENTAL PATHWAYS AND DISTRIBUTION
EXPOSURE OF HUMANS AND OTHER BIOTA
HEALTH AND ENVIRONMENTAL EFFECTS
RISK CONSIDERATIONS

Note: Solid lines indicate direct flows of information; dotted lines indicate selective data inputs.

FIGURE 3-1 OVERVIEW OF ENVIRONMENTAL RISK ASSESSMENT PROCESS

the assumptions and limitations of the risk assessment approach. Subsequent chapters of this report discuss each of these components in more detail.

3.2 INITIAL CONSIDERATIONS IN A RISK ASSESSMENT

The initial considerations of a risk assessment include:

- Establishment of the scope and focus of the risk assessment.
- Identification of the subject material to be considered in highest priority and with greatest detail.
- Development of a work plan and/or approach for completing the risk assessment.

This component initiates the risk assessment process by providing a basis for understanding the requirements of the risk assessment, and an organization for the work conducted throughout the risk assessment process. To avoid unnecessary effort and development of data on topics of little significance, it is essential to carefully define the desired goals and outcome of the specific risk assessment. The scope should be established in terms of the parameters described earlier--scale, populations considered, time frame, potential effects, and intended use of the assessment.

Once the initial scope and focus of the risk assessment have been defined, the next step is to determine in general terms the type and availability of information for the risk assessment process. This can be accomplished through brief literature reviews, consultation with experts, analysis of recent reviews on particular chemicals, etc. Next, priority areas of investigation are identified, for example, a specific pathway, a specific set of health effects, an industry of significance, etc. Priorities should be set according to the overall requirements of the risk assessment and the expectations of availability of information.

Following prioritization of areas of investigation, the final step in the initial considerations is to develop a work plan for conducting the risk assessment. The work plan should estimate the effort devoted to each of the major components, indicate the major areas of information flow and exchange, and establish a timetable for the conduct of the risk assessment.

After several risk assessments have been performed, the initial considerations component will become a "natural process." Nevertheless, it will still be important to identify the overall goals of the risk assessment, establish priorities, and develop a work plan to increase the potential for achieving those goals.

3.3 MATERIALS BALANCE (ENVIRONMENTAL LOADING)

The objectives of the materials balance component are:

- To identify the important (if not all) pollutant sources
- To identify the chemical and physical form of the pollutant, as it is released to the environment.
- To characterize the environmental loading of the pollutant--quantities, geographic locations, rates, receiving environments.
- To identify uses and releases of the pollutant leading to direct exposure.
- To achieve a balance between production and uses or releases.
- To establish the confidence or uncertainty of data on releases of the pollutant.

The materials balance approach requires a systematic identification of sources, estimates of environmental releases, and characterization of the receiving environment. A comprehensive analysis may be enhanced through a checklist or ordered procedure for examining all aspects of the processes of generation and release of the pollutant. Figure 3-2 shows an example checklist, indicating a source matrix and an environmental input matrix. All types of manufacturing processes, transportation, storage, and disposal activities, as well as uses of the pollutant or products containing the pollutant should be considered. Specific processes, uses and releases, and the environmental compartments receiving the release that can lead to direct exposure potential should be identified. As a check on the quantification of releases, the degree of closure of the materials balance (the relationship of production, import, export, use, disposal, and environmental release data) is established. The ranges of uncertainty in environmental releases of data for the pollutant should also be established; several approaches for this task are discussed in Section 4.3.

The materials balance is often a difficult component of the risk assessment to perform since there are many production processes, transportation and storage procedures, and use patterns that affect releases to the environment. Processes may not be described, uses may be unknown, and quantitative data on releases may not be available. Thus, in many cases, engineering estimates will have to be made in order to describe likely or expected environmental releases. The assumptions and uncertainties associated with all environmental releases should be documented wherever possible. Those releases that can result in direct exposure of persons or other biota to the pollutant should be highlighted as this information will be directly used in the environmental pathways and distribution analysis, as well as the exposure and health effects analyses.

SOURCE MATRIX

ENVIRONMENTAL INPUT MATRIX

EXTRACTION

		WATER				
		QUANTITY	RATE	FORM	LAND	AIR
Extraction Method	Type of Release					
drilling strip mining	routine accidental					

MANUFACTURING

Manufacturing Processes	Material Class	Type of Release					
chemical reactions digestion	contaminant by-products/ co-products primary product	routine accidental					

TRANSPORTATION

Disposal					

FIGURE 3-2 EXAMPLE OF MATERIALS BALANCE CHECKLIST

3.4 MONITORING DATA

Goals of the monitoring data component of the risk assessment are:

- To identify concentrations of the pollutant in all environmental media.
- To determine the geographical and temporal distribution of the pollutant in these media.
- To identify geographical locations and other factors associated with pollutant releases to the environment and to provide data on possible exposure of humans and other biota.

This component often begins with a comprehensive review of literature including access to available computerized environmental data bases, such as those discussed in Section 6.3. From these data, average ambient and effluent concentrations in air and water may be established; concentrations in soil, sludges, plants, animals, fish tissues, foods, drinking water, etc., should be determined, evaluated, and summarized. It is important to identify, wherever possible, the uncertainties in experimental or analytical data. Some of the more common problems with monitoring data include: uncertainties in the chemical/analytical procedures used, confidence levels, and detection limits; uncertainties in obtaining representative samples of the environmental media; the lack of data on the temporal variations in concentrations at different locations; uncertainties in the chemical or physical forms of the pollutant; and the lack of sufficiently detailed and/or extensive data. Despite these limitations, monitoring data can provide an indication of the locations of pollutant releases to the environment, a potential means for assessing exposure of humans and other biota, and a direct means of confirming the materials balance and the environmental pathways and fate analysis.

3.5 ENVIRONMENTAL PATHWAYS AND DISTRIBUTION

If the environment and the pollutants were "static" and adequate monitoring data were available, materials balance and monitoring data, combined with information on receptor distribution could be used to estimate exposure of humans and other biota to pollutants. However, the environment is not static--pollutants are transported, undergo transformation, accumulate and degrade--and the actual environmental distribution of a pollutant is different from that associated directly with environmental releases. The environmental fate and pathways component of a risk assessment is directed at estimating the actual distribution of the pollutant in the environment. Specific goals of environmental fate and pathways component are numerous:

- To define environmental compartments of importance.
- To identify important transport mechanisms; physical, biological, and chemical transformation processes, and predominant chemical forms of the pollutant.
- To summarize transfer and reaction rates, controlling processes and lifetimes of the pollutant in the environment.
- To trace pollutant pathways from sources to sinks.
- To estimate pollutant concentrations in different environmental media and their time dependence.
- To compare the results of the pathways and fate analysis with monitoring data.
- To establish relationships between releases to the environment and exposure.

A variety of approaches may be used in environmental fate and pathways analysis; qualitative estimates may be based upon case examples or environmental scenarios, simple analytical equilibrium or transport models, or complex multi-media models. The materials balance component provides inputs; evaluation of physical, chemical, and biological fate processes defines the persistence of the pollutant in the environment; and models are used to estimate environmental concentrations. Figure 3-3 shows one approach to pathway analysis. In utilizing environmental models, it is important to assess average concentrations in environmental media of broad geographical distribution, as well as environmental pathways and resultant concentrations in specific localized areas. The output of the fate and pathways analysis should yield pollutant concentration distributions in sufficient spatial and temporal detail to allow estimates of exposure of humans and other biota.

For many environmental situations, adequate models do not exist or are just now under development. Furthermore, for new or uncommon chemicals, many of the physical, chemical, and biological properties needed to estimate transformation rates, persistence, and distribution are not available. For example, few models exist to predict adequately the distribution of pollutants released from the landfill into ground water and surface water. Models to estimate residual concentrations of pollutants in edible foods resulting from the land disposal of sludges, contaminated irrigation water, pesticide or nutrient application, dry deposition, are in very early stages of development. Therefore, uncertainties and limitations of the models should be identified, and estimates of pollutant distribution based upon materials balance, fate and pathways analysis should be compared with monitoring data.

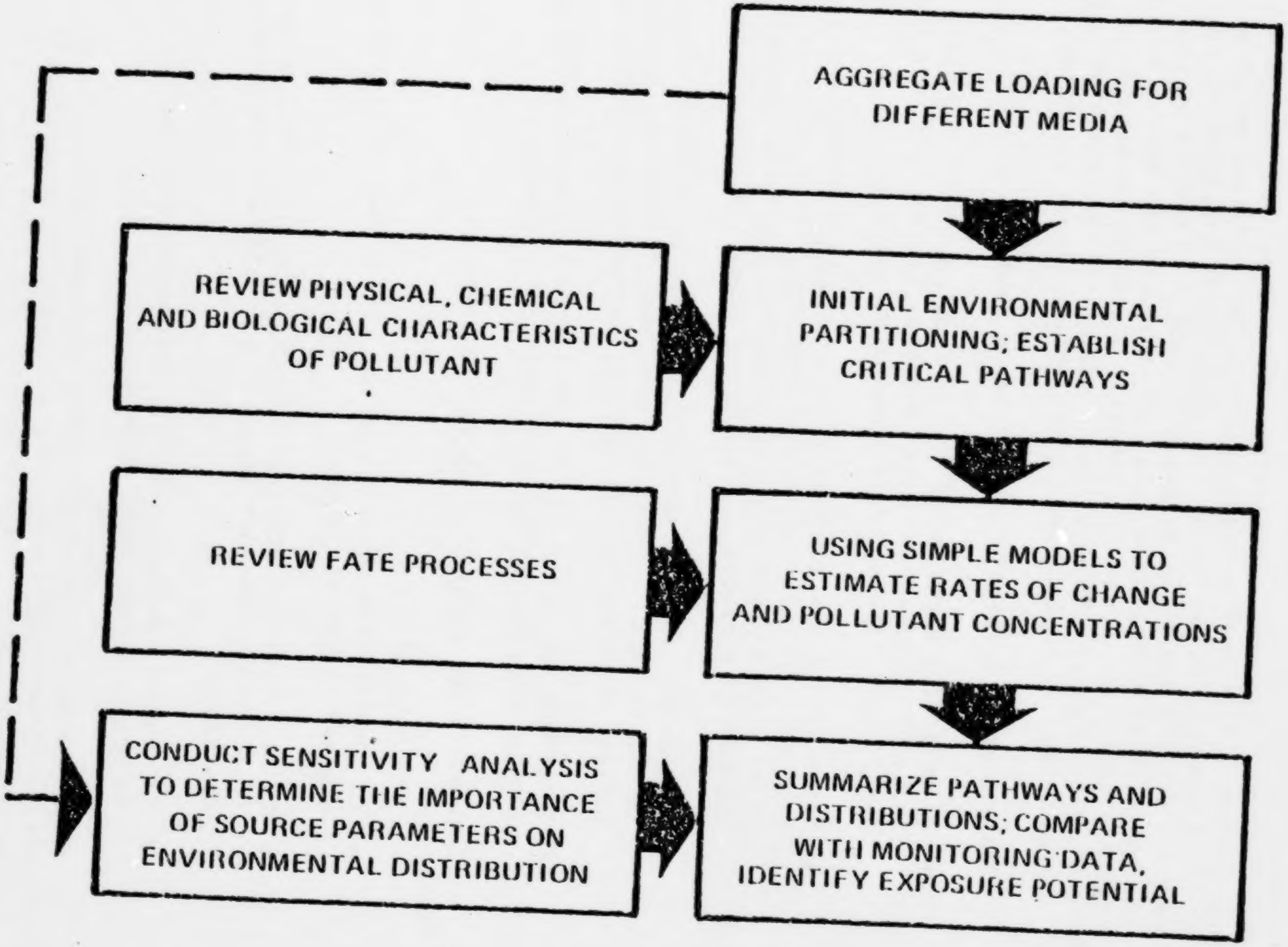

AGGREGATE LOADING FOR DIFFERENT MEDIA
REVIEW PHYSICAL, CHEMICAL AND BIOLOGICAL CHARACTERISTICS OF POLLUTANT
INITIAL ENVIRONMENTAL PARTITIONING; ESTABLISH CRITICAL PATHWAYS
REVIEW FATE PROCESSES
USING SIMPLE MODELS TO ESTIMATE RATES OF CHANGE AND POLLUTANT CONCENTRATIONS
CONDUCT SENSITIVITY ANALYSIS TO DETERMINE THE IMPORTANCE OF SOURCE PARAMETERS ON ENVIRONMENTAL DISTRIBUTION
SUMMARIZE PATHWAYS AND DISTRIBUTIONS; COMPARE WITH MONITORING DATA, IDENTIFY EXPOSURE POTENTIAL

FIGURE 3-3 SCHEMATIC EXAMPLE OF FATE AND PATHWAYS ANALYSIS

3.6 EXPOSURE OF HUMANS AND OTHER BIOTA

The analysis of exposure of humans and other biotic population groups to pollutants is one of the most difficult and critical elements of the risk assessment process. In general, there is no well established methodology or body of literature on exposure. The combinations of exposure routes, durations, extents, and the numbers and locations of persons or organisms exposed may be large and difficult to identify or characterize. Also, there is usually a wide range of estimated and actual exposures corresponding to the nature and behavior of the subpopulation groups. However, estimates of exposure are essential, since otherwise the risks of the pollutant to various population groups cannot be ascertained.

The principal goals of human exposure analysis are:

- To determine exposure of the general public to the pollutant in terms of pollutant sources, exposure routes, exposure durations and frequencies, exposure amounts or extents.
- To determine the exposure of the workplace population to the pollutant in terms of occupations, types of facilities or operations, the numbers of workers exposed and their characteristics, the exposure routes, durations, frequencies, amounts or extents.
- To identify specific subpopulation groups in terms of geographic location, size, occupation, age, sex, dietary or recreational habits, with higher than typical exposures to the pollutant.
- Determine the exposure of individuals in these subpopulation groups in terms of the aforementioned parameters.

Similarly, the general goals for exposure analysis of biotic populations are:

- To identify the types, location, and number of biotic species exposed to the pollutant.
- To determine the exposure routes, exposure durations and frequencies, exposure amounts or extents for the exposed species.
- To quantify as best possible the exposure of various species to the pollutant under consideration.

Although no well established exposure methodologies exist, a systematic approach to identifying and quantifying exposure is essential to the process. All routes of exposure, i.e., ingestion, inhalation, and dermal absorption, must be included. Subpopulations should be identified with specific sources and exposure routes, for example, those populations drinking ground or surface water, urban and rural population groups, those with unique dietary patterns, using products containing the pollutants, or those who reside near sources or disposal operations. In establishing exposure, it is important to identify the characteristics of the population exposed; the duration and frequency of the exposure; the range, average and maximum, of actual or potential exposure for individuals in the population group that lead to estimates of daily intake for average individuals and those who belong to special population subgroups.

The inputs to the analysis of exposure come from the materials balance; monitoring data for ambient air and water; concentrations in foods; results of pathways analysis; physiologic data such as respiratory rate, average drinking water intake, etc.; and the use of models or data which relate average daily intake by different exposure routes to total body burden of the pollutant. It is frequently convenient to display exposure data in a matrix form listing various routes of exposure, exposure parameters, and estimated or observed intakes for the general population and those for extremes in population subgroups. Figure 3-4 shows an example matrix, partially completed for a hypothetical pollutant.

Throughout the analysis of exposure, it is important to identify data gaps and uncertainties in data. For example, there will frequently be data on occupational inhalation in the workplace, but limited data on inhalation for the general public residing near a workplace situation where a pollutant is used. Environmental fate and monitoring data may be helpful in these situations. Similarly, models may be needed to relate dermal absorption of pollutants when the pollutant is found in water used for washing, swimming, or other recreational purposes, etc. In considering waterborne pollutants, it will be important to identify population groups with varying sources and quality of drinking water, since this route is one of the most significant exposure routes. Similarly, data from market basket surveys, other food, fish tissue, and pesticide residue studies, will also be needed to assess exposure through food ingestion. Food ingestion can be considered a waterborne route of exposure since water is used for irrigation of crops, preparation of food, and as the environmental media normally associated with fish and shellfish in the diet.

With regard to exposure of aquatic organisms and other biota, there are usually few data available to quantify exposure. Monitoring data and examination of bioaccumulation data provide the best sources of information on possible exposure of various species. Data on populations of aquatic and other biota, where available, can then be associated with potential concentrations of the pollutant in the water environment in order to estimate potential and actual exposure of organisms to the pollutant. A systematic approach considering ingestion and absorption exposure routes should be utilized for aquatic species; inhalation, ingestion and absorption exposure routes should be considered for terrestrial species.

Population/ Size	Route	Subpopulation/ Associated Source	Exposure Concentration	Exposure Constant	Exposure Duration/ Frequency	Calculated Intake
General	Ingestion	Drinking Water typical maximum	e.g. 10 μg/ℓ 110 μg/ℓ	Adult – 2 liter per day Children – 1 liter per day	regular daily	
		Food typical maximum	e.g. 10 ppb 100 ppb		once per week	
	Inhalation	Urban – typical maximum	e.g. 4 μg/m^3 25 μg/m^3	Infant 4 m^3/day child 12 m^3/day adult 29 m^3/day	continuous	
		Rural – typical maximum	e.g. 1 μg/m^3 5 μg/m^3			
	Dermal Absorption	Water – typical maximum	e.g. 100 μg/ℓ 1 mg/ℓ		once per week daily	

FIGURE 3-4 HUMAN EXPOSURE MATRIX

3.7 EFFECTS ON HUMANS AND OTHER BIOTA

The overall goal of a human health effects analysis is to identify and characterize the adverse health effects in humans that are known or expected to occur as a result of exposure to a pollutant. Specific goals of human health effects analysis are:

- To evaluate acute and chronic health effects in humans resulting from exposure to the pollutant based upon occupational or accidental exposures and/or human epidemiological studies.
- To evaluate the acute and chronic health effects in humans based upon review of *in vitro* and *in vivo* studies with laboratory animals, test organisms, tissues, cell cultures, or other biota.
- To examine the distribution, metabolism, bioaccumulation and excretion of pollutants in humans and laboratory animals to identify effects mechanisms and relationships between dose and response.
- To estimate dose-response relationships in humans based upon epidemiological, accidental human data, extrapolation of laboratory animal data and to estimate "no effects" levels in humans.

Similarly, the goals of analyzing effects on other biota are:

- To identify concentrations of pollutants that have adverse effects on individual species and communities of aquatic and terrestrial organisms.
- To identify and evaluate the acute, chronic, and reproductive effects in various species as functions of exposure level.
- To identify factors that influence the availability of a pollutant to biota.

The general approach used to perform the human health effects analysis includes literature search, analysis of epidemiological and laboratory studies, evaluation of studies of metabolism, absorption, and bioaccumulation, summarization of acute and chronic health effects, and development of dose-response relationships for both acute and chronic effects. In undertaking health effects analysis, all serious adverse effects on humans should be considered. These include acute and subchronic effects, chronic effects such as carcinogenicity, mutagenicity, teratogenicity, fetotoxicity, and functional disorders and effects of critical organ systems--central nervous, reproductive, hepatic, renal, cardiac, gastrointestinal, respiratory, digestive, circulatory systems, etc. In addition, studies of metabolism, absorption, bioaccumulation and excretion should be evaluated to help understand the relationships between various exposure routes and health effects, and to establish if animal models are suitable for extrapolation to humans. In undertaking these analyses, it would be desirable if data were available on humans from epidemiologic studies or information on accidental exposures. Frequently, however, these data are not available and reliance must be placed on extrapolation of laboratory animal data. For many chemicals, animal data are not available and only reports of *in vitro* data exist. If no data are available on a pollutant, inferences may be drawn from data on related pollutants, using due caution. Examination of structure activity relationships of various pollutants may provide information if other data are not available.

Wherever possible, multiple studies using different species of laboratory animals should be utilized. Several methods of extrapolating dose-response in animals to dose-response in humans should be explored and the results of these extrapolations compared with any available epidemiologic or accident data. Throughout the analysis and extrapolation procedures, uncertainties and assumptions used should be identified and quantified. If possible, the end result of the human effects analysis should be the development of quantitative relationships between dose and response of humans and a clear explanation of the data and rationale leading to these relationships. In performing a risk assessment, it may not be necessary to examine all types of health effects if only certain exposure routes are applicable. Thus, in the initial considerations of a risk assessment, it will be important to identify major exposure routes so that the effects analysis can proceed in a direct and straightforward manner.

An analysis of the effects in non-human species can be accomplished through data collection and preliminary data review, followed by critical data evaluation and summary reporting of the effects. Data should be collected on both laboratory studies measuring the effects of pollutants on various species and field investigations or case studies documenting actual effects of the pollutant in the environment. Information on fish-kills, field reproduction studies, and other field data can be especially important in verifying effects predicted from laboratory studies. It is important to understand the experimental conditions of laboratory tests of effects so that effects parameters such as LD_{50} or LC_{50} can be extrapolated to potential field environmental conditions. Following preliminary data collection, a critical review should be accomplished. Lethal and sublethal, acute and chronic effects should be examined for fish and aquatic invertebrates in fresh and salt water and marine and estuarine species. Important parameters influencing the results such as pH, temperature, water hardness, type of bioassay, exposure time, etc., should be considered. The effects of different exposure routes should be examined. Toxicity to terrestrial plants through root uptake of pollutants in the soil and toxicity to animals through ingestion of contaminated biota and water should be examined. The effects of the pollutant on species in the human foodchain should also be evaluated. After these data have been evaluated, they can be summarized to identify sensitive aquatic or terrestrial species, "no effects" concentrations, dose-response relationships, and conditions which influence environmental effects for a number of important species.

The end result of the effects analysis for both human and non-human species is a comprehensive summary of health effects data including uncertainties and ranges in dose-response relationships, and applicability of the effects data to various potential routes and to real environmental situations.

3.8 RISK CONSIDERATIONS

The overall goal of the risk considerations component is to develop a qualitative and/or quantitative understanding of the nature, extent, and severity of the risks imposed by a pollutant on humans, fish, wildlife and other biota. The specific goals are:

- To estimate the average health risks to the general human population based upon average exposures and ranges of health effects effects associated with the pollutant.
- To estimate the extent and severity of health risks associated with the pollutant in specific human subpopulations that sustain greater than average risks.
- To estimate the average risks to general populations of fish, shellfish, wildlife, and other species based upon average exposure and the range of effects associated with the pollutant.
- To estimate the extent and severity of risks to subpopulations of fish, shellfish, wildlife and other species that sustain higher than average risks.
- To identify sources, pathways and causal factors associated with risks for human and other species in order to understand possible methods for risk reduction.

As indicated earlier, the combination of exposure and health effects are required to estimate risk to various species. In evaluating the risks of an environmental pollutant, a single result will usually not occur; rather a risk assessment will describe a spectrum of risks for subpopulations, characterized by the type of adverse effect and the exposure of the subpopulations over time. In identifying and evaluating risks, it is important to determine whether the acute or chronic toxic effects and exposures are quantifiable, or whether qualitative measures must be used. Depending upon the degree of quantification, outcomes of the risk consideration include: (1) qualitative indications of possible risks; (2) estimates of risk for hypothetical exposure levels; (3) estimates of risks using conservative assumptions on health effects, or (4) quantitative assessment of risk for subpopulations via various exposure routes.

Several approaches include: a qualitative comparison of exposure levels with "no effects" or "lowest effects" levels to indicate the general nature of risks to humans and other biota; a semi-quantitative analysis using safety factors and application of daily intake and health effects data to result in a better defined range of risks for various exposures of humans; a quantitative risk analysis to predict, with clear identification of the inherent assumptions, mortality or morbidity resulting from exposure of general and subpopulation groups to the pollutant. For example, the output of the risk consideration component may indicate that a margin of safety of 100 or 1000 exists between typical average exposures of humans and known or extrapolated effects levels. Another possible output would be an estimation of the range of numbers of tumors resulting from exposure of the general human population to a known carcinogenic pollutant. Similarly, in terms of biotic risks, the output of the risk consideration component could include either comparison of effects levels for various species with exposure concentrations or, if possible, quantitative analysis of mortality of various aspects as a result of exposure.

In summarizing risk considerations, the uncertainties present in exposure and effects data should be addressed. The basis for the effects and exposure data should be carefully examined and confidence levels established, if possible. Risk quantification for chronic health effects is often particularly difficult to express.

In order to assist the regulatory process, it is appropriate to analyze the risks associated with various exposure routes or exposure scenarios so that the benefits from environmental regulation or control can be ascertained.

3.9 PRESENTATION OF RISK ASSESSMENTS

An important element of the risk assessment process is the clear, thorough, and well-documented presentation of data and results in a manner which can be understood by scientists, technical experts, regulators, and the public. Although it is difficult to address the needs of these varied audiences, attempts should be made to provide information in the risk assessment report in various levels of detail, geared to different readers. Frequently it will be necessary to use secondary sources of information; but references should be clear and complete. It will be important to present information so that other investigators can examine the validity of the assumptions, data, calculations, and results for future studies. Only if the risk assessment report is prepared in sufficient detail, with sufficient clarity, will it be most useful for the purposes intended.

4.0 MATERIALS BALANCE--SOURCE IDENTIFICATION AND LOADING ESTIMATION

4.1 INTRODUCTION

A thorough understanding of the distribution of a pollutant in the environment is essential to determining the likelihood that humans and other biota will be exposed to it and the magnitude of the exposure. In principle, the distribution of a pollutant can be established by two methods:

(1) review, analysis, and interpretation of available environmental monitoring data; and

(2) development of estimates of sources and loadings (discharges or inputs to the environment) of the pollutant, coupled with analysis of environmental pathways and fate of the pollutant.

For some well-studied pollutants, existing monitoring data may be sufficient to provide a comprehensive view of environmental distribution. However, for most pollutants, and particularly for new chemicals or recently identified pollutants, extensive monitoring data are not available and the environmental distribution must be estimated. Furthermore, environmental monitoring data alone are not sufficient to establish the effects of alternative regulatory control strategies on the potential risks associated with pollutants since monitoring data do not always provide positive correlations between pollutant sources and environmental distribution. Since certain chemical or product uses may lead to direct exposure, assessment of the sources, uses, and environmental loadings of a pollutant is an important first step in a comprehensive exposure analysis.

In the context of this exposure analysis methodology, the term "materials balance" is defined as a description of the flow of a pollutant from its generation through its initial release to one of the environmental compartments (air, water, land). Production and use, source identification, and pollutant loading studies are often called materials balances, depending upon the scope and nature of the work conducted. A comprehensive materials balance analysis involves other evaluations as well, including the pollutant's transport, storage, common and uncommon uses, and eventual disposal.

The concept of a materials balance is illustrated in Figure 4-1, which depicts a pollutant (or product in which a pollutant is a contaminant) at various stages in its life cycle. The pollutant (product) is first extracted from the natural environment or synthesized, and after initial transportation and/or storage, may be further manufactured, processed, or transported in many more stages than are shown in the figure. Other key steps in the life cycle are stages of use and disposal of the pollutant (product). The interior of the large box in the figure represents processes generally conducted in the cultural or anthropogenic environment.

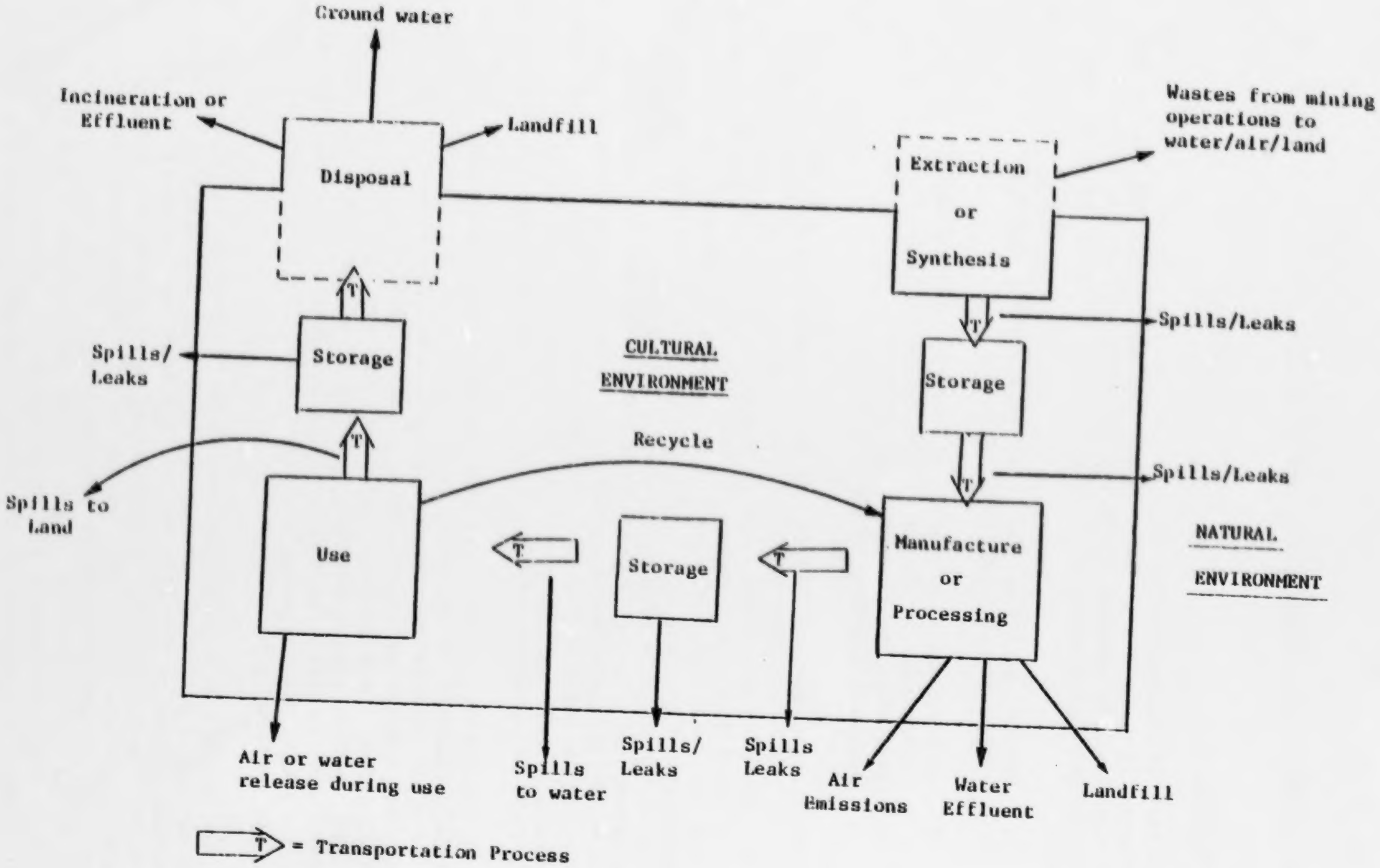

Ground water
Incineration or Effluent
Landfill
Disposal
Wastes from mining operations to water/air/land
Extraction or Synthesis
Spills/Leaks
Storage
Spills/Leaks
CULTURAL ENVIRONMENT
Storage
Spills/Leaks
Recycle
Spills to Land
Use
T
Storage
T
Manufacture or Processing
NATURAL ENVIRONMENT
Air or water release during use
Spills to water
Spills/Leaks
Spills Leaks
Air Emissions
Water Effluent
Landfill
T = Transportation Process

FIGURE 4-1. GENERALIZED MATERIALS BALANCE FLOW DIAGRAM SHOWING TYPICAL RELEASES

At any step within the cultural environment, the pollutant may be released to the natural environment (represented by the space outside of the large box), e.g., to air, land, water, biota, etc. The releases may be planned and controlled (e.g., a permitted discharge to the air or a receiving waterbody), or accidental and uncontrolled (e.g., a spill from a rail car or storage tank into the soil or water, or runoff or leaching from abandoned mining sites). The materials balance is more complex when natural sources of the pollutant already exist in the environment, independent of human activity. For completeness, significant natural sources must be incorporated in the materials balance, although achieving closure or balance of sources, uses, and releases is far more difficult when a large reservoir already exists in the environment.

Product use may result in a direct exposure of humans or other biota, for example, lead in paint, cosmetics, cigarettes, etc. In addition, environmental releases may also result in direct exposure of humans or other biota, for example, a release in the workplace. In other situations, the pollutant must be redistributed in the environment (e.g., into drinking water or biota such as fish) prior to exposure. Thus a complete materials balance can provide insights into potential exposure, as well as the data necessary for estimation of environmental distribution.

4.2 GOALS OF A MATERIALS BALANCE

The overall goal of the materials balance portion of these exposure analyses is to obtain a complete and quantitative description of the uses and sources of a pollutant and a characterization of the form and mode of entry of the pollutant into the environment. A complete materials balance should:

(1) Describe the types of uses and use situations, especially for consumers.

(2) Identify all existing and potentially significant sources of the pollutant.

(3) Identify the chemical and physical form of the pollutant as it enters the environment.

(4) Characterize (qualitatively and, where possible, quantitatively) the entry of the pollutant into the environment (loadings) in terms of: amounts, seasonality, geographic locations, rates, receiving environments.

(5) Identify uses and environmental releases that can lead to direct exposure of receptors.

(6) Account for all material produced by achieving a balance between the amount produced naturally, inadvertently and by industry, and the amount transformed, contained (unavailable for release), stockpiled, and released to the environment.

(7) Establish the confidence and/or uncertainties in the amounts of pollutant releases by various sources to the environmental compartments.

Ideally, a materials balance effort would address all potential, as well as existing, pollutant sources. This may not be practicable because of both data and resource limitations. Given these limitations, it is tempting to focus first on the identification of major existing uses, though sources deemed insignificant on a national scale may be very significant in selected areas. Therefore, care must be taken in limiting the scope of the analysis.

A systematic approach to source identification can aid this process; many possible sources must be considered in order to determine which are the most important by virtue of their national or local significance or the opportunity for direct receptor exposure. The physical and chemical form of the pollutant as it enters the environment are important because these characteristics affect the significance of various environmental pathways and the resultant distribution.

The spatial (geographic, source intensity) and temporal (rate and frequency of release) characteristics of the environmental loading must be considered. Total pollutant quantities involved and the characteristics of the receiving medium are also important. This information will ultimately be used to determined the environmental distribution. Depending upon the scope of the risk analysis (e.g., local, regional or national), quantification of releases may not be necessary. Both documented data and engineering estimates may form the basis for quantification, when it is desirable or possible.

Understanding and delineating the uncertainties in source and loading estimates, i.e., determining confidence limits, increases their usefulness in the subsequent steps in environmental risk analysis, and any regulatory control recommendations ultimately derived. Similarly, achieving closure of the materials balance--i.e., equating all of the production or input of the pollutant with use, accumulation, destruction, or release of the pollutant to the environment--makes the subsequent risk analysis more comprehensive, substantive, and credible. The level to which these goals and objectives may be achieved will depend upon the availability of data, the nature of the pollutant, and the effort that can be devoted to this portion of the risk analysis.

4.3 MATERIALS BALANCE METHODS

There are two major steps in performing a materials balance--the first is a thorough identification of sources and the second is quantification of loading/emission rates to the specific receiving compartments of the environment. Environmental pathway analysis (see Chapter 5.0) can then be used to establish transfers and reactions of the pollutant within and among environmental compartments, which, in turn, determine environmental concentrations and influence exposure. Therefore, the data developed from the materials balance must be compatible with the requirements of environmental pathway and exposure methodologies. The major challenges in developing a materials balance are the identification of sources, assembly of data, and quantification of loadings for pollutants that are not reported in the literature or are unknown or unquantified because of the lack of control technology.

The general approach for a materials balance is shown in the flow chart in Figure 4-2. Key validation issues are: data completeness and uncertainty, materials balance closure, and compatibility with the needs of subsequent components of risk assessment. At many points in the analysis, the need for better and/or additional data may arise. Judgments regarding the value of higher quality information must be made in order to determine whether engineering estimates or continued literature review for direct measurements will be required.

The first step is to establish the goals and scope of the materials balance effort, including the desired outputs of the work and criteria for determining when this portion of the risk analysis has been completed in sufficient detail. Next, the analysis should be focused on a qualitative description of the flow of the pollutant within the cultural environment and potential releases to the natural environment. This step should highlight the unique character of the pollutant and indicate areas requiring extensive data gathering and analysis. The description should cover the complete range of industrial processes that involve the pollutant: extraction, processing, storage, uses of the pollutant or product containing the pollutant, and all potential disposal modes. The greater the number of processes, the greater and more varied are the potential opportunities for release to the environment and the more complicated and potentially incomplete may be the analysis, due to insufficient data. Knowledge of major uses of a product, product lifetimes, and disposal processes may become important in establishing total environmental releases; these data are likely to be difficult to obtain for the entire range of possible products and uses.

A materials balance matrix, such as is shown in Table 4-1 for phthalate esters (Perwak et al. 1981a), provides a convenient method for initially organizing data on pollutant sources and loadings. Ideally such a matrix provides a logical framework for a thorough accounting of sources. The matrix consists of a source axis for identification of points of release, and an environmental input axis for estimating and organizing loading factors or rates for each source. The matrix includes the processes relevant to establishing source identification, e.g., extraction, refining, manufacturing, processing, transportation, storage, use, or disposal (see Table 4-2) and suggests materials classes and types of releases to be considered. It also provides a framework for allocating and aggregating pollutant releases to environmental compartments of air, land, water and biota and listing data on quantities, rates and forms of release.

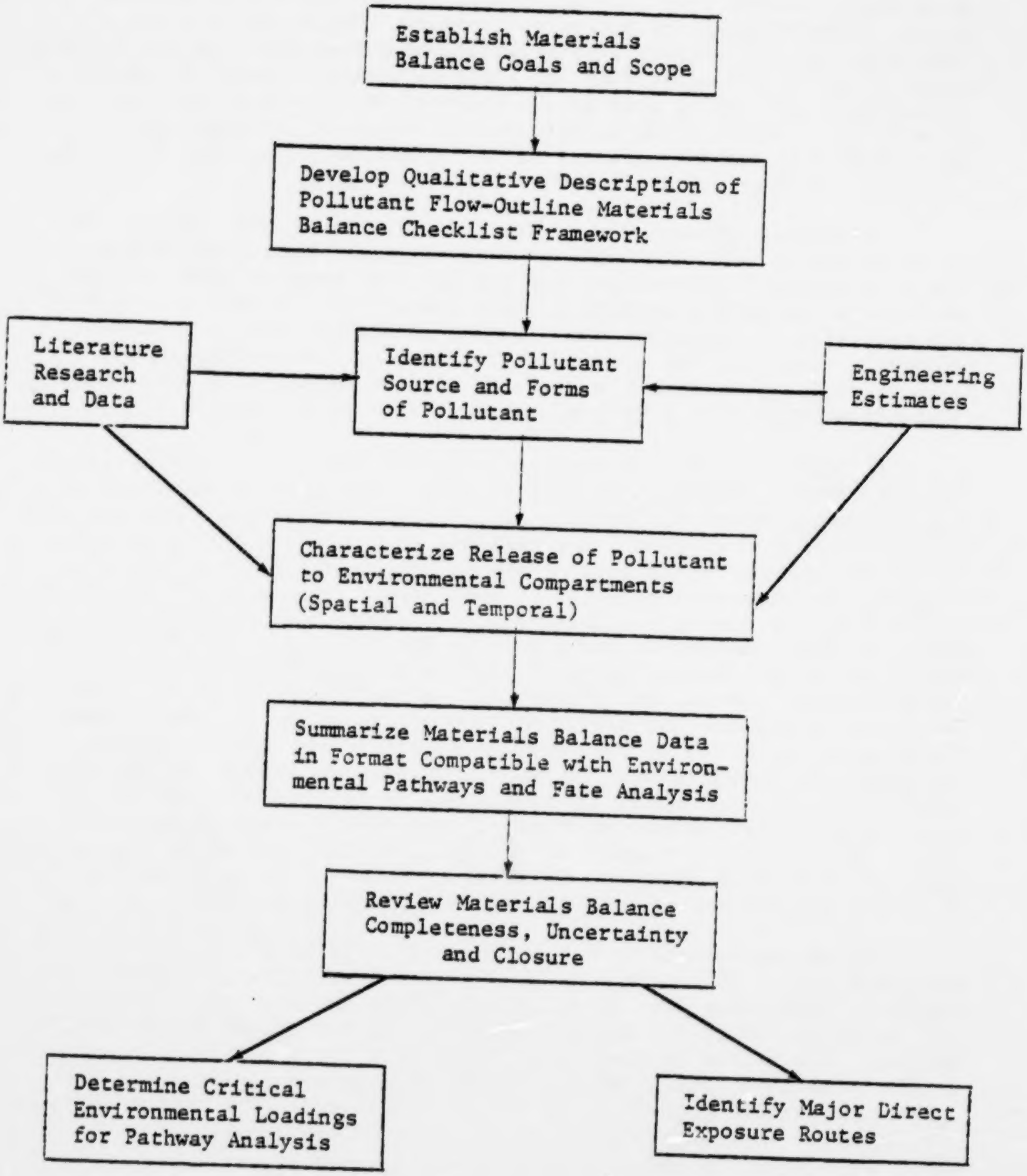

Establish Materials Balance Goals and Scope
Develop Qualitative Description of Pollutant Flow-Outline Materials Balance Checklist Framework
Literature Research and Data
Identify Pollutant Source and Forms of Pollutant
Engineering Estimates
Characterize Release of Pollutant to Environmental Compartments (Spatial and Temporal)
Summarize Materials Balance Data in Format Compatible with Environmental Pathways and Fate Analysis
Review Materials Balance Completeness, Uncertainty and Closure
Determine Critical Environmental Loadings for Pathway Analysis
Identify Major Direct Exposure Routes

FIGURE 4-2. MATERIALS BALANCE METHODOLOGY FLOW CHART

TABLE 4-1. EXAMPLE OF SOURCE AND ENVIRONMENTAL LOADING MATRIX: PHTHALATE ESTERS

1977 Total Phthalate Ester Production 545.9
Exports 42.5
U.S. Supply 503.4

(thousand kkg/yr)

	(A) Fraction of Total Phthalate Ester Production	(B) Amount of U.S. Supply	(C) Transportation Related Loss @ 0.1%		(D) Fraction in Various Use Categories		(E) Fraction in Product Category		(F) Amount DXE (B-C)	(G) Vaporized During Compounding @ 3.0%	(H) Manufacture Waste Factor, 98% Land, 2% Incinerated	(I) Waste .97 x H x F	(J) Remaining Amount F-G-I	(K) Release Rate/Year for Product in Use	(L) Amount Released per Year in Use	(M) Average Lifetime (Years)	(N) Total Released during Product Lifetime	(O) Remaining for Disposal 97% to land, 3% burned	Annual Flux: Released to air .35 G + K	Annual Flux: Released to Water G + .65 G + N	Annual Flux: Landfilled (I + O) x .97	Annual Flux: Incinerated (I + O) x .03	
DEHP	0.2	167.6	0.2	Non-plasticizer	-		-		-	-	-	-	-				-	-	-	0.2	-	-	
				Other polymers	.05		1.0		8.4	0.3	0.02	0.6	7.7				?	8.6	0.1	0.2	7.9	0.1	
				PVC plasticizer	0.6																		
				Direct contact with liquids		swimming pool liners	0.016	.035	5.6	0.2	0.02	0.2	5.2	0.005 to water	0.1	5	0.3	4.9	0.1	0.4	5.0	0.2	
						garden hoses	0.010																
						medical uses	0.11																
				Film in contact with air		flooring	.226	.655	106.2	1.1	0.03	2.4	93.7	0.001 to air	0.2	10	1.9	91.8	1.0	2.0	96.2	[illegible]	
						weather stripping	.015																
						furniture	.112																
						wall covering	.060																
						auto mats & tops	.033																
						auto upholstery & seat covers	.112																
						apparel	.100																
						food wrap	.015																
				Low surface contact		wire & cable	.181	.110	49.1	1.5	0.02	1.9	45.9	0.002 to air & water	0.1 0.1	7	0.6 0.6	44.6	1.2	1.6	45.0	1.6	
						housewares	.018																
						sport goods & toys	.041																
						other PVC uses	.065																
										Incinerated wire & cable		[illegible] 1.8							4.4	4.4	64.1	5.1	DEHP
BBP	0.1	55.4	0.1	Non-plasticizer	-				- -	- -	-	-	-	-					-	0.1	-	-	
				Other polymers	.15		1.0		8.3	0.1	0.02	0.4	7.6	?	?	?	?	7.6	0.1	0.2	7.8	0.2	
				PVC plasticizer	.85	vinyl flooring	.900		42.1	1.1	0.01	0.6	40.7	0.001 to air	0.1	10	0.8	19.8	1.3	0.8	19.0	1.2	
						other PVC uses	.100		4.7	0.1	0.01	0.1	4.2	?	?	?	?	4.2	0.05	0.1	4.6	0.1	
																			1.45	1.2	31.2	1.5	BBP
DBP	0.01	7.0	0.01	Non-plasticizer	.05		1.0		0.4	-	?	?	0.4	0.2 air 0.2 water	0.1 0.1	1	0.1 0.1		0.1	0.1	0.1	--	
				Other polymers	.50		1.0		1.5	0.1	0.02	0.1	1.1	?	?	?	?	0.1	0.06	0.1	3.3	0.1	
				PVC plasticizer	.45	direct contact grp	.035		0.1	0.001	0.02	0.004	0.1	0.005 water	0.001	5	0.005	3.3	-	0.01	0.1	0.005	
						contact w/air grp	.655		2.1	0.1	0.01	0.2	1.9	0.001 air	0.006	10	0.06	0.1	0.1	0.04	1.9	0.1	
						low surface contact	.310		1.0	0.01	0.02	0.06	0.9	0.002 air water	0.002 0.002	7	0.01 0.01	1.8 0.9	0.02	0.01	0.9	0.01	
																			0.26	0.28	6.1	0.235	DBP
DEP	0.01	7.5	0.01	Non-plasticizer	.05		1.0		0.4	-	?	?	0.4	0.2 air 0.2 water	0.2 0.2	1	0.2 0.2		0.2	0.2	0.1	-	
				Celluloseics	.95		1.0		7.2	0.2	0.02	0.1	6.7	?	?	?	?	0.1 6.7	0.1	0.1	6.7	0.2	
																			0.3	0.3	6.8	0.2	DEP
DMP	0.004	4.0	0.004	Non-plasticizer	.30		1.0		1.2	-	?	?	1.2	0.2 air 0.2 water	0.5 0.5	1	0.5 0.5		0.5	0.5	0.2	0.01	
				Celluloseics	.70		1.0		2.8	0.1	0.02	0.1	2.6	?	?	?	?	0.2 2.6	0.01	0.1	2.7	0.1	
																			0.51	0.6	2.9	0.11	DMP
DNOP	?	?	-	-	-		-		-	-	-	-	-	-	-	-	-	-	-	-	-	-	DNOP

Source: Perwak, J., et al. An exposure and risk assessment for phthalate esters. Final draft report. Contracts EPA 68-01-3857, 5949. Washington, DC: Monitoring and Data Support Division, Office of Water Regulations and Standards, U.S. Environmental Protection Agency; 1981.

NOTE: DEHP = di(ethyl hexyl)phthalate; BBP = butyl benzyl phthalate; DBP = dibutyl phthalate; DEP = diethyl phthalate; DMP = dimethyl phthalate; DNOP = di-n-octyl phthalate

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TABLE 4-2. SOURCE IDENTIFICATION FOR MATERIALS BALANCE MATRIX

Extraction Method

drilling, dredging, strip or pit mining wastes (slags, to air, water or other)

Refining Operations

washing, grinding, extraction, distillation, physical separation wastes

Manufacturing Process

chemical reaction, cracking, digesting, forming wastes (pollutants in form of primary product, by product or co-product, or containment)

Processing

extrusion, molding, calendaring, drying, pressing, cutting wastes

Transportation

loading/unloading, cleaning, in transport (volatilization, leaks) by truck, by rail, by plane, contained in tank cars, drums, disposal sacks

Consumptive Use

industrial, commerical, household, institutional, or agricultural uses in which pollutant is confined/contained, applied (e.g., swimming pool. agriculture) or consumed in products

Naturally or Inadvertently Occurring

In minerals and soils, in aquatic systems, in air, in biota, volcanic activity, formation in upper atmosphere, natural combustion; inadvertent release from urban runoff, or use of pollutant-bearing products (e.g., fossil fuels, cement or other)

Disposal Methods

POTW, septic systems, solid waste landfill, contained landfill, incineration, deep well injection, discharge (treated or untreated) to surface waters including lakes, streams or ocean, or deposition in "sealed" drums

The source and environmental input categories may be further subdivided depending upon the pollutant and the scope of the materials balance. For example, the environmental input may be subdivided by geography (e.g., urban versus non-urban), by depth of environmental medium (e.g., surface water versus groundwater), or by waterbody type (natural: streams, lakes, estuarine or coastal waters; versus manmade: effluents, reservoirs, or sewers). Deposition on soil may occur as the result of aqueous discharges through leaching, adsorption, or sediment transport. The relative contributions of these processes may need to be considered and the matrix may have to be expanded accordingly.

Expansion of the matrix to include receptors as they interact with receiving media would aid in classifying the relative importance of receiving media. For example, the receptors may be people, fish, game, livestock, crops or materials, most of which will have specific interaction zones with various classes of emissions (e.g., people exposed in the workplace or through product use at home). Consideration of these interactions would be particularly useful in identifying direct exposures to a pollutant.

After possible sources, uses, and releases have been arrayed, the next step is to develop and summarize data concerning sources and loadings. The data abstracted from the open scientific literature and from government publications or contractor reports may be supplemented by data from industrial product literature, trade journals, or popular periodicals and reports. A list of commonly available and reliable data sources is presented in Chapter 10.

In general, one can expect considerable data gaps and, therefore, a high degree of uncertainty in the materials balance for ubiquitous and naturally occurring priority pollutants, for pollutants entering a variety of media from numerous sources, and for new chemical pollutants or newly recognized toxicants. Quantitative data may be lacking for various common source categories and estimation will have to be relied upon to fill the data gaps. Estimations made from chemical or industrial engineering data will often be based on product levels, emission factors, anticipated spill frequencies, etc. Different sources of data and estimation procedures will probably be required for each process listed in the materials balance checklist. Assumptions made in the estimate should be clearly stated so that uncertainties can be identified and checked at a later time, if appropriate.

The structure and approach to environmental fate analysis (for example, whether or not computer models are used) will also help to define the materials balance matrix. The appropriate scales for time and geographical regions will become evident by the nature of available data or as the available data are reviewed. Wherever possible, the materials balance data should include identification of the physical/chemical state (i.e., phases, chemical complexes, oxidation state, etc.) of the substance in products and releases. In many risk analyses, considerable interaction between the environmental pathways and the materials balance components will be required with each continually refined as a result of considerations arising from the other. Data describing the geographical distribution of sources and loading rate characteristics are generated according to the information needs of air dispersion, stream flow, groundwater, or lake models used in pathway analysis.

After data have been summarized, it is important to review the results for completeness, close of balance, and uncertainty. Assessment of completeness is subjective, since additional literature research or investigation may lead to new data or estimates. Judgments will have to be made as to whether more effort should be expended in developing additional data on other sources or loadings. Examination of the degree of closure of the materials balance may be useful in making these judgments. This will involve comparing all of the pollutant generation steps or inputs with pollutant releases or outputs over a selected time frame. If inputs agree well with outputs, greater certainty in the completeness of the materials balance has generally been achieved.

There is some uncertainty associated with most, if not all, calculations and value determinations involved in developing a materials balance, largely due to varying limitations on monitoring data, on assumptions associated with approximations of pollutant release from different processes or activities, and on simulation models. Sufficient monitoring data, which is current and of high quality, will reduce the magnitude of uncertainty associated with a materials balance. However, there are many components involved in a materials balance and typically good monitoring data are available only for a few, if any.

Three approaches are available for evaluating the uncertainty in materials balance calculations in order to establish some degree of confidence in the results. The first is a parametric approach based on a mathematical model linking the input and output variables. In this approach, ranges of input values (e.g., 100-200 kkg/year) are assigned (through educated judgment or sensitivity analysis) and partial derivatives are the principal tool in the parametric analysis. The second approach is statistical in that parameters are statistically estimated from the available data. Uncertainty associated with a parameter in this approach is expressed in terms of a statistical confidence interval, that is, the range within which the true value of the parameter is expected to lie (e.g., 100 ± 50 kkg) with an assigned degree of confidence. As there is uncertainty associated with each parameter or dependent parameter, the uncertainties can be combined by the method of error propagation to obtain the confidence of the output variable. These two approaches are described in more detail by Serth et al. (1978) and are currently being studied by the Exposure Assessment Group of the Office of Health and Environmental Assessment, U.S. EPA.

A third approach is a qualitative one in which uncertainty is assigned to materials balance calculations on the basis of educated judgment. The resulting uncertainty can be defined: in terms of expected ranges; as the most likely of several values calculated by different methods; or as a qualifying statement associated with one approximation, e.g., under x conditions, it is very likely that pollutant release from this source will be y.

The outputs of the materials balance are several: the source and environmental input matrices, containing data on sources and loadings; identification of large or critical environmental loadings and related characteristics, which can serve as the basis for environmental pathway scenarios/analyses; and identification of major routes for direct exposure for use in human and nonhuman exposure analyses.

4.4 EXAMPLES OF MATERIALS BALANCE OUTPUT

4.4.1 Introduction

The examples in this section are presented in order to illustrate the extent to which a materials balance for a particular pollutant can be focused to characterize the predominant sources of the environmental burden. As previously mentioned, materials balances may quantify releases of a specific chemical that result from its commercial or inadvertent production, its transportation or use, transportation or use of a product in which it is a component, or natural sources. The three materials balances discussed below - those for chloroform, copper, and pentachlorophenol - are all different in their focus.

Examples drawn from the materials balance section of the chloroform exposure and risk assessment (Perwak et al. 1980a) illustrate the approach used to develop meaningful environmental release data for inadvertent sources since the burden of chloroform in the aquatic environment originates primarily from its production during chlorination rather than from commercial releases. The materials balance illustrations from the copper exposure and risk assessments (Perwak et al. 1980b) address quantification of the environmental burden of an abundant natural material. The third example detailed in this section is taken from the pentachlorophenol exposure and risk assessment (Scow et al. 1980) where the estimation of environmental releases associated with the ultimate use of materials containing pentachlorophenol was a major challenge.

4.4 EXAMPLES OF MATERIALS BALANCE OUTPUT

4.4.2 Chloroform

Two major reference documents provided the initial conceptual framework and much of the data necessary to developing a materials balance for chloroform (Perwak et al. 1980a); a large study the National Academy of Sciences completed in 1978 and a study by a contractor for the U.S. Environmental Protection Agency, released in draft form in 1980. The study by the National Academy of Sciences was completed soon after the health hazards of chloroform were initially recognized and hence did not have the advantage of being able to draw upon the substantial body of research that has been done subsequently. Therefore, some of the conclusions drawn by NAS researchers had to be reevaluated in light of the more recent work. The very recent U.S. EPA contractor report treated the commercial processes that generate chloroform in great detail but did not contain much information useful for purposes of developing a materials balance focused on the releases to the environment.

Unlike the situation with chemical substances that are exclusively man-made, the literature concerning chloroform has noted several significant sources of chloroform releases that originate outside of commercial production or consumption of the chemical. Since 80-95% of commercially produced chloroform is consumed by chemical reaction as feedstock for chlorodifluoromethanes and is not available for release to the environment, the indirect and natural sources of chloroform account for the majority of environmental releases.

Estimates of the production rates for indirect sources vary widely, and for some of the sources, there are a number of subcategories that have not all been clearly or consistently defined. For example, water is chlorinated for several different purposes, including cooling purposes, disinfection of potable water or swimming pools, and water treatment within publicly owned treatment works (POTWs); each has different rates of generation and release and different geographic distribution. Available estimates of the magnitudes of these chloroform sources are conflicting or, in some cases, there are no estimates whatsoever. In order to resolve conflicting data and to fill data gaps, it was necessary to distinguish between causative relationships (between sources and environmental releases of chloroform) and coincident occurrences (e.g., what is the source of chloroform in coastal waters--chlorinated sewage effluent, production by marine algae, or both?).

Detailed knowledge of industrial processes and the chemical industry structure were required in order to generate estimates of source strength. For example, calculations based on industry interviews (combined with values reported in various symposia) resulted in an estimate of 12,500 MT per year of chloroform produced by the pulp bleaching industry. The values previously reported for this release ranged from 1 MT per year in the U.S. to 300,000 MT per year worldwide. Actually, part of the total release occurs during the bleaching process inside the pulp plant and part occurs during treatment of the plant effluent. Some data were available concerning the chloroform release during effluent treatment stages, but very few data were available for releases during other stages of the bleaching process and, therefore, the best available approximation had to be pieced together from interviews with industry experts.

The ultimate measure of success of a materials balance study must be the degree of closure obtained between the sources and use/releases of the chemical. The results obtained for chloroform are displayed in Table 4-3 and Figure 4-3. As indicated, the "unaccounted for" amount is equal to more than 50% of the amount known to be released to the environment. However, there are also uncertainties regarding the amount of chloroform commercially produced and the amount devoted to the major consumptive use (F-22 feedstock). Therefore, after laboratory use and stockpiles are taken into account, nearly all of the "unaccounted for" amount could conceivably result from the uncertainty in the production volumes.

4.4.3 Copper

Copper is one of the more abundant metals among the 129 priority pollutants and as such has many sources of significant environmental releases. Data are generally available concerning releases from many of these sources for incorporation into the materials balance for copper (Perwak, et al. 1980b). A materials balance for copper is shown in Tables 4-4 and 4-5 and Figure 4-4.

Copper is mined and milled in seven states, and effluent discharges and solid waste disposal practices have been monitored in order to determine the compliance with current environmental regulations. With these data, releases from mining and milling can be estimated for the known production volumes of the respective mills, based on approximate recovery and waste treatment efficiencies.

TABLE 4-3. EXAMPLE OF MATERIALS BALANCE OUTPUT INVOLVING INADVERTENT RELEASES--ESTIMATED PRODUCTION AND USE/RELEASES OF CHLOROFORM, 1978

Production (kkg)

Commercial Production		159,000
Methyl Chloride Process	122,500	
Methane Process	36,000	
Loss during Production	500	
Imports		7,670
Production as Contaminant		2,733
Vinyl Chloride Monimer	2,679	
CH_3Cl, CH_2Cl_2, and CCl_4	54	
Chlorination of Water		3,466
Cooling Water	2,460	
Potable Water	912	
POTW*	91	
Swimming Pools	3	
Bleaching of Paper Pulp		12,500
Automobile Exhaust		965
Photodecomposition of Trichloroethylene		450
Marine Algae		(unknown)
		186,784

TABLE 4-3. EXAMPLE OF MATERIALS BALANCE OUTPUT INVOLVING INADVERTENT RELEASES--ESTIMATED PRODUCT AND USE RELEASES OF CHLOROFORM, 1978 (Continued)

Uses/Releases (kkg)	Air	Water	Land		
Feedstock for F-22 Production					142,700
Exports					7,900
Destroyed/Retained in Products/Storage					3,968
VCM Products				2,290	
Pharmaceutical Production				1,610	
F-11/F-12 Production (and others)				47	
$CHCl_3$ Production				17	
Pesticide Production				4	
Unaccounted for (including laboratory use and stockpiles)					11,600
Released to Environment	19,207	912	496		20,615
Pulp & Paper Bleaching	12,100	400	--		
Chlorination of Water	3,245	221	--		
Pharmaceutical Extractions	1,525	275	290		
Automobile Exhaust	965	--	--		
$CHCl_3$ Production	370	14	6		
Trichloroethylene Decomposition	450	--	--		
VCM Production	187	2	200		
Transportation & Storage Loss	177	--	--		
F-22 Production	150	--	--		
Pesticides	38	--	--		
					186,783

*Publicly Owned Treatment Works

Source: Perwak, J. et al. An exposure and risk assessment for trihalomethanes. Final Draft Report. Contract EPA 68-01-3857. Washington, DC: Monitoring and Data Support Division, Office of Water Regulations and Standards, U.S. Environmental Protection Agency; 1980.

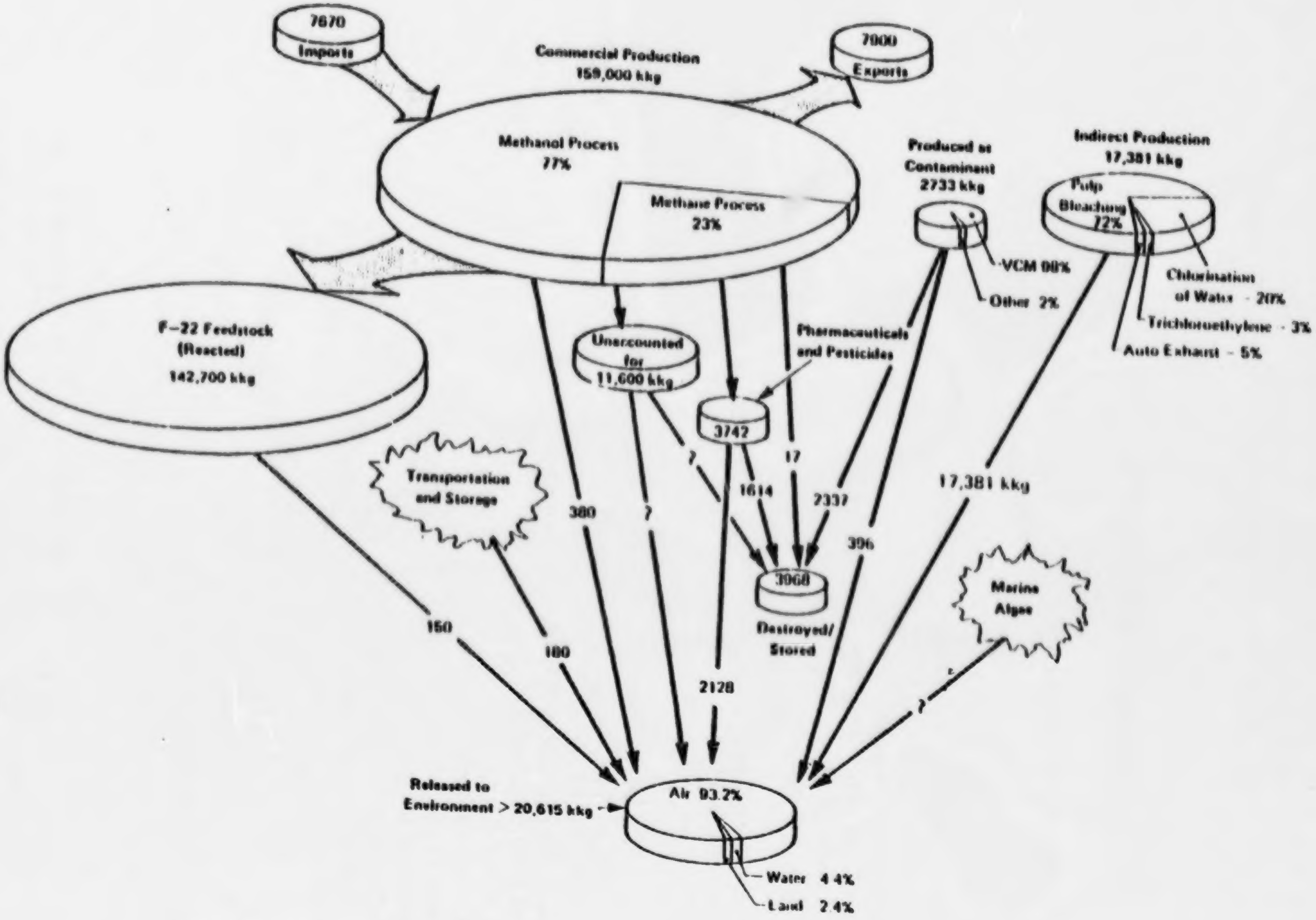

7870
Imports
Commercial Production
159,000 kkg
7000
Exports
Methanol Process
77%
Methane Process
23%
F-22 Feedstock
(Reacted)
142,700 kkg
Unaccounted for
11,600 kkg
3742
Pharmaceuticals and Pesticides
3968
Destroyed/
Stored
Produced as Contaminant
2733 kkg
VCM 98%
Other 2%
Indirect Production
17,381 kkg
Pulp Bleaching
72%
Chlorination of Water - 20%
Trichloroethylene - 3%
Auto Exhaust - 5%
Transportation and Storage
Marine Algae
150
180
380
?
?
1614
17
2337
2128
396
17,381 kkg
?
Released to Environment > 20,615 kkg
Air 93.2%
Water 4.4%
Land 2.4%

FIGURE 4-3 EXAMPLE OF GRAPHIC PRESENTATION OF MATERIALS BALANCE OUTPUT--ENVIRONMENTAL LOADING OF CHLOROFORM, 1978

Source: Perwak, et al. An exposure and risk assessment for trihalomethanes. Final Draft Report. Contract EPA 68-01-3857. Washington, DC: Monitoringand Data Support Division, Office of Water Regulations and Standards, U.S. Environmental Protection Agency; 1980.

TABLE 4-4. EXAMPLE OF COMMERCIAL PRODUCTION AND USE DATA--SUMMARY OF U.S. COPPER SUPPLY AND DEMAND, 1976

Source/Consumer	Supply (MT)	Consumption (MT)
Domestic mine production and beneficiation	1,287,940	
Refined Scrap	204,080	
Unrefined Scrap	149,660	
Imports (refined)	235,810	
Imports (ores-concentrates)	99,770	
Industry Stocks, 1 January 1976	419,940	
Copper Wire Mills		1,349,288
Brass Production		567,092
Other		39,110
Industry Stocks, 31 December 1976		441,710
Total	2,397,200	2,397,200

Note: The above figures are for one year (1976). There is considerable statistical variation from year to year; consequently, these do not reflect average values.

Source: Perwak, J. et al. An exposure and risk assessment for copper. Final Draft Report. Contract EPA 68-01-3857. Washington, DC: Monitoring and Data Support Division, Office of Water Regulations and Standards, U.S. Environmental Protection Agency; 1980

TABLE 4-5. EXAMPLE OF MATERIALS BALANCE OUTPUT INVOLVING NATURAL SOURCES-- U.S. ESTIMATED ENVIRONMENTAL RELEASES OF COPPER, 1976

Source	Release (MT/yr) Air	Direct Aquatic	POTW	Land
Primary Production	Δ	13.4^{2}	-	1,078,290^{2}
Smelting	200^{2}	Unknown		Unknown
Secondary Production	Δ	0.3^{3}	7^{3}	Δ
Metallic Ore Mining & Related Activities	Δ	34^{3}	-	Unknown
Copper Wire Mills	164^{1,2}	134^{1}	1,484^{1}	Δ
Brass Production	3^{1,2}	151^{1}	294^{1}	42^{1,2}
Iron & Steel Production	17^{1,2}	656^{3}	-	896^{1,2}
Coal Mining**	Δ	181^{1,2}	-	-
Pulp, Paper & Paperboard	-	110^{3}	-	-
Inorganic Chemicals	-	4^{3}	-	-
Steam Electric Industry	-	174^{3}	-	-
Machinery Mfgr.	Δ	151^{1}	-	-
Electroplating		400^{3}	1,400^{3}	920^{3}
Miscellaneous Sources	-	72^{3}	-	-
Area Sources:				
Abandoned Metal Mines	-	314^{9}	-	-
Agricultural Applications	*	3,600^{5}	*	19,195^{4,5,6}
Urban Runoff	-	441^{2}	84^{2}	*
Suspended Sediment	-	18,400^{2}	-	-
Incineration/Refuse	100^{2}	-	-	1,900^{2}
POTW	-	2,073^{9}	-	9,680^{8}
Total	484	26,909	3,269‡	1,110,923

^{Δ}Insignificant

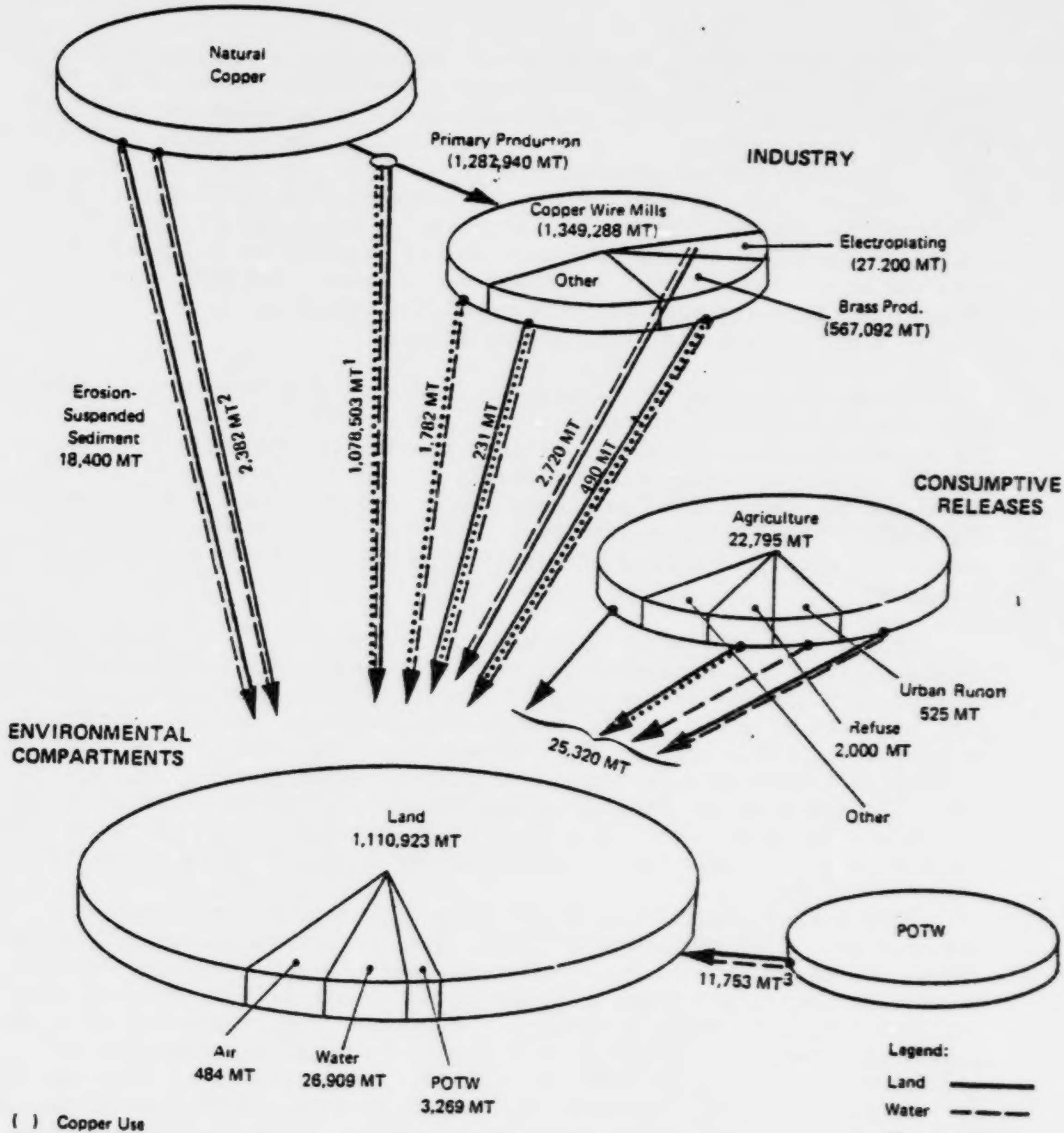
*These emissions are directly applied to the category in which they are reported; however, often during or shortly following release, they enter other environmental media.

**Coal combustion is known to release some copper; insufficient data is available to substantiate this quantity.

‡The total estimated POTW influent is 11,800 MT/yr (see Table 6). Thus, only a portion of the sources have been identified.

[1] Versar, 1978.
[2] Arthur D. Little Estimate.
[3] Effluent Guidelines Monitoring Data, analyzed by Versar, EPA, 1979.
[4] U.S. Department of Agriculture, 1974.
[5] SRI, 1979.
[6] EPA, 1974.
[7] EPA, 1977.
[8] Table 6.
[9] Martin and Mills (1976).

Source: Perwak, et al. An exposure and risk assessment for copper. Final Draft Report. Contract EPA 68-01-3857. Washington, DC: Monitoring and Data Support Division, Office of Water Regulations and Standards, U.S. Environmental Protection Agency; 1980


Natural Copper
Primary Production (1,282,940 MT)
INDUSTRY
Copper Wire Mills (1,349,288 MT)
Other
Electroplating (27,200 MT)
Brass Prod. (567,092 MT)
Erosion-Suspended Sediment 18,400 MT
2,382 MT[2]
1,078,503 MT[1]
1,782 MT
231 MT
2,720 MT
490 MT
CONSUMPTIVE RELEASES
Agriculture 22,795 MT
Urban Runoff 525 MT
Refuse 2,000 MT
Other
25,320 MT
ENVIRONMENTAL COMPARTMENTS
Land 1,110,923 MT
Air 484 MT
Water 26,909 MT
POTW 3,269 MT
POTW
11,753 MT[3]
Legend:
Land
Water
Air

( ) Copper Use

[1] Includes smelting

[2] Industrial releases in which copper exists as a trace element. Sources include iron and steel production, coal mining, pulp and paperboard manufacture, steam electricity generation, other ore mining, and abandoned mines.

[3] POTW effluent includes contributions from human and other unknown sources.

Note: Boundaries between receiving medium are often undefined and/or changing: Copper apparently released to one compartment can result in another.

FIGURE 4-4 EXAMPLE OF GRAPHIC REPRESENTATION OF MATERIALS BALANCE OUTPUT--ENVIRONMENTAL LOADING OF COPPER, 1976

Source: Perwak et al. An exposure and risk assessment for copper. Final Draft Report. Contract EPA 68-01-3857. Washington, DC: Monitoring and Data Support Div., Office of Water Regulations and Standards, U.S. EPA; 1980

As with many of the metals, copper occurs in the natural environment in combination with other elements. The release associated with the mining and milling of these related ores can be assessed from information on the nature and scale of production, the level of sophistication of recovery and waste treatment technology, the frequency with which it is applied, and the availability of documentation and monitoring data on all of the above. Copper is a significant by-product/co-product of lead-zinc deposits, occurs in coals, and is released as a consequence of iron and steel production. For these major associated production processes, EPA documentation and other published research data were available to quantify the resulting copper release.

Copper is consumed in a variety of uses ranging from brass production to electroplating to agricultural applications (as an algicide). The Bureau of Mines annually publishes reports concerning the distribution of copper and other mined minerals in the U.S. economy. The U.S. Bureau of the Census also publishes import-export data for all inorganic chemicals. These sources provide a baseline for estimating releases associated with the various stages of production and use of copper (Table 4-4).

Frequently, information concerning treatment efficiencies or general disposal practices can provide the basis for estimating environmental releases. For example in the case of brass production, effluent guidelines data provided by the U.S. EPA were used to estimate aquatic discharges of copper from this source; the computed total fell within the realm of reasonable losses as a percentage of copper consumption in this application. In the case of electroplating, however, estimated releases based on the available Effluent Guidelines Data (or continuing data source of the U.S. EPA) exceeded the amount of copper consumed by that industry.

This overestimation can be attributed to some of the underlying assumptions. Electroplaters do not always operate on a regularly scheduled basis, nor is their volume of production consistent. Many are "captive" operations contained within a larger industry and produce only to meet the needs of that parent industry. Independent electroplaters also use copper somewhat intermittently since some materials are plated with nickel, silver, zinc, or some combination. Therefore, a release estimate for the materials balance based on "averaged" values from limited sampling of electroplating effluents would be incorrect. Bureau of Mines staff and industrialists familiar with the electroplating industry were consulted in order to approximate the waste recovery efficiency and the maximum possible percentage of material loss.

A significant source of copper to the environment is through POTWs which receive influent from urban runoff, industrial discharge, and domestic and commercial units. A contractor study performed for the U.S. EPA provided removal efficiencies of metals for a "representative" sampling of POTW influents and effluents for primary, secondary and advanced treatment facilities. This information was combined with data concerning total treated effluent from POTWs in the United States and outlying territories and an assumed distribution of treatment levels (2% of the flow from primary treatment plants, 64% from secondary and nearly 35% from advanced).

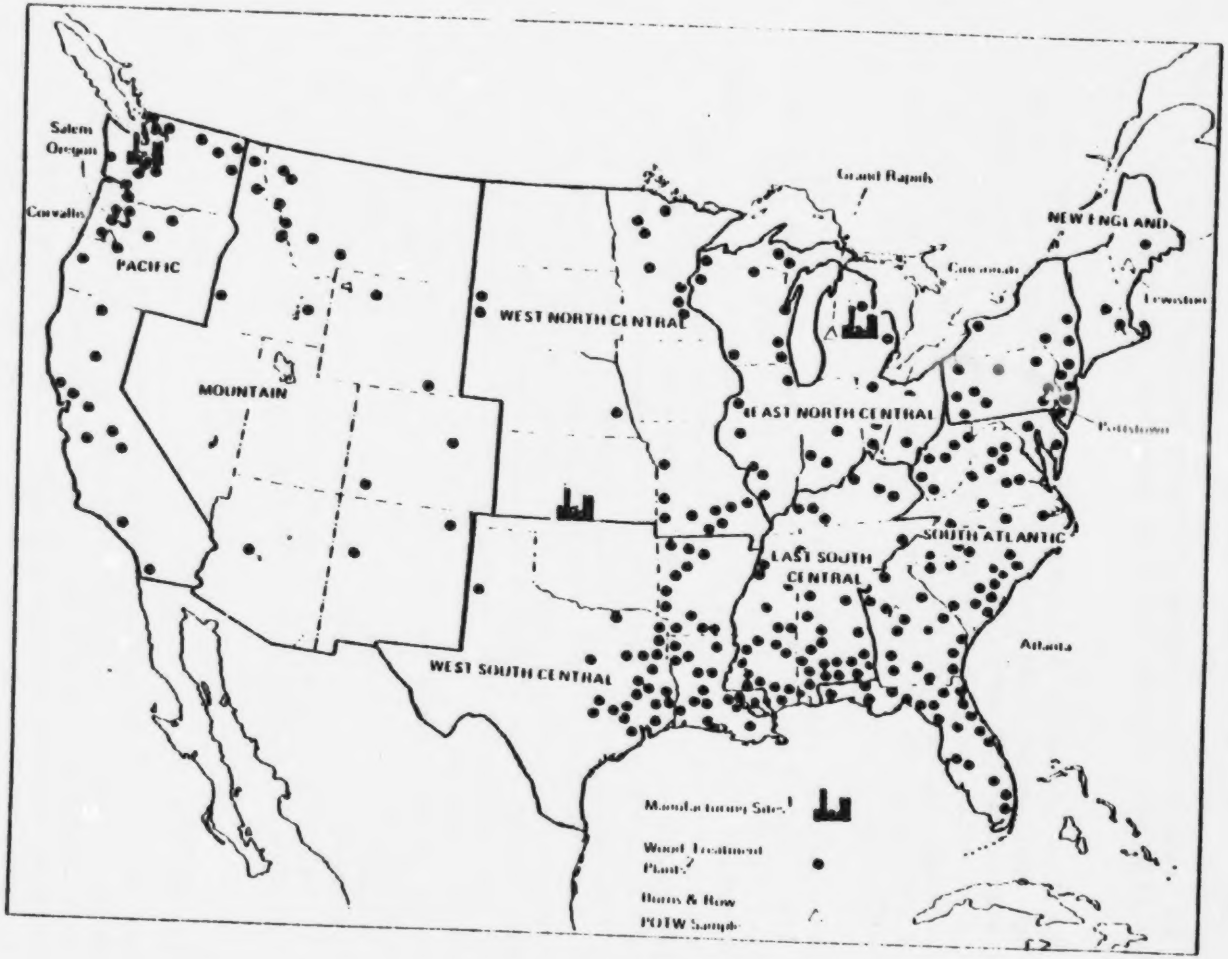
A problem remained, however, in identifying the sources of copper in POTWs. Average residential loading of 42 mg Cu/day/person was assumed on the basis of samplings from sewer systems in St. Louis and Cincinnati. Residential areas provided roughly one-third of the copper to POTWs. Adequate data on commercial and industrial contributions were not available to permit a determination of the source of the remaining 66% of the copper in POTW influent.

Whenever environmental releases are arrayed and totalled, care has to be taken to avoid double counting. The best example from the materials balance for copper is the case of urban runoff. The volume of copper carried by urban runoff was determined from stream samples of urban runoff to separate storm sewers, point sources, and unsewered areas. Possible sources of copper released to the urban environment that would be reflected in runoff include exposed construction elements, transportation vehicles, industrial applications (plumbing, tubing, valves, etc.) and settled particulates from atmospheric releases (e.g., coal burning power plants). This latter source has already been accounted for as an air release. Clearly, though some of the atmospheric copper releases are also included in the concentrations in runoff, separating these from the other components of urban runoff is very difficult. Urban runoff itself may flow to a POTW, so that there is opportunity for triple counting the original releases to air. Often, as was the case in the copper materials balance, insufficient data are available to permit differentiating the relative contributions of individual sources of a pollutant to urban runoff and POTWs. Although instances of double counting cannot always be avoided, they do result in uncertainties in the analysis and need to be identified.

4.4.4 Pentachlorophenol

Pentachlorophenol (PCP) is commonly used throughout the United States as a wood preservative and its characteristics and applications are fairly well known to this industry. As a result, much of the information included in a materials balance for this pollutant came from specialists in the timber and wood products industries, as well as from U.S. EPA contractor reports and water quality programs. In comparison with materials balance analyses of others of the 129 priority pollutants, the PCP materials balance (Scow et al. 1980) was quite simple and straightforward due to the nature of both the manufacture and use of this compound.

At the present, PCP is manufactured at three locations in the U.S., as shown in Figure 4-5, by three different chemical companies. Each


Salem Oregon
Corvallis
PACIFIC
MOUNTAIN
WEST NORTH CENTRAL
Grand Rapids
EAST NORTH CENTRAL
Cincinnati
NEW ENGLAND
Lewiston
Pottstown
SOUTH ATLANTIC
EAST SOUTH CENTRAL
WEST SOUTH CENTRAL
Atlanta
Manufacturing Sites1
Wood Treatment Plants2
Burns & Roe POTW Sample

Notes: 1. Battelle for EPA, 1975
2. Forest Service, U.S. Department of Agriculture

FIGURE 4-5 EXAMPLE OF GEOGRAPHIC DISTRIBUTION OF PRODUCTION SOURCES--LOCATIONS OF PENTCHLOROPHENOL MANUFACTURING AND WOOD TREATMENT PLANTS

Source: Scow et al. An exposure and risk assessment for pentachlorophenol. Final Draft Report. Contract EPA 68-01-3857. Washington, DC: Monitoring and Data Support Division. Office of Water Regulations and Standards, U.S. Environmental Protection Agency; 1980.

facility produces PCP by the same process during which phenol is chlorinated in the presence of a catalyst. During production, releases occur to the air and to water. Air emissions are limited by a scrubber mechanism enabling PCP recovery; incentives for control of atmospheric release are economic, as well as regulatory. At the time of the pentachlorophenol study (1980), industry production of pentachlorophenol was not subjected to regulatory control by the U.S. EPA; sampling data on aquatic discharges were not available. In addition, there were no reliable data on the efficiency of the production process with respect to aquatic discharge upon which gross annual discharge estimates could be based. Most of the PCP that is domestically produced is consumed in the U.S. and there are no identified imports.

The wood preserving segment of the timber industry consumes more PCP than all other users combined. Though consumption varies from year to year, wood preserving consumes roughly the same share of total production each year: an estimated 78% (U.S. EPA timber industry) to as high as 85% to 93% (chemical industry). When applied to wood, pentachlorophenol enhances toughness, prevents discoloration, and prevents attack by wood-destroying fungi and insects. The timber industry is a relatively mature U.S. industry and as such is well established and fairly well known. For this reason and because of the industry's dominating consumption of PCP, 78% to 93% of manufactured PCP can be fairly well traced through its lifetime of wood-associated uses.

The timber industry reports that 415 wood preserving plants operated by 300 companies potentially use PCP. These plants are geographically located on Figure 4-5, in a pattern consistent with the major timber resources of the nation. Associated consumption of PCP by wood preserving plants is shown in Figure 4-6 as it is distributed to six regions of the U.S. At this stage, wood is impregnated with PCP and there are small releases to POTWs and some to land. Most aquatic discharges from wood preserving plants occurs during a wood conditioning process prior to application of PCP.

Following PCP application, waste streams at 90% of the 415 wood preserving plants are evaporated so that there is no aquatic discharge at all. Of the remaining 10%, most use a stream process to apply PCP treatment and treat their wastewaters with roughly 81% efficiency resulting in a discharge of 5.1 MT of PCP to POTWs (Scow et al. 1980). The other plants use the Boulton process to treat wood and treat their wastewaters with a 44% efficiency (Scow et al. 1980) consequently discharging 0.2 MT of PCP to POTWs. Only one small wood treatment plant discharges its waste stream directly to surface waters. This facility operates on an intermittent basis (less than 25 days per year) discharging less than 26.5 kg annually. Most of the PCP released by wood preserving plants is contained in sludge, and these releases were estimated to be 74.5 MT per year on the basis of sludge practices and removal efficiencies (Scow et al. 1980).

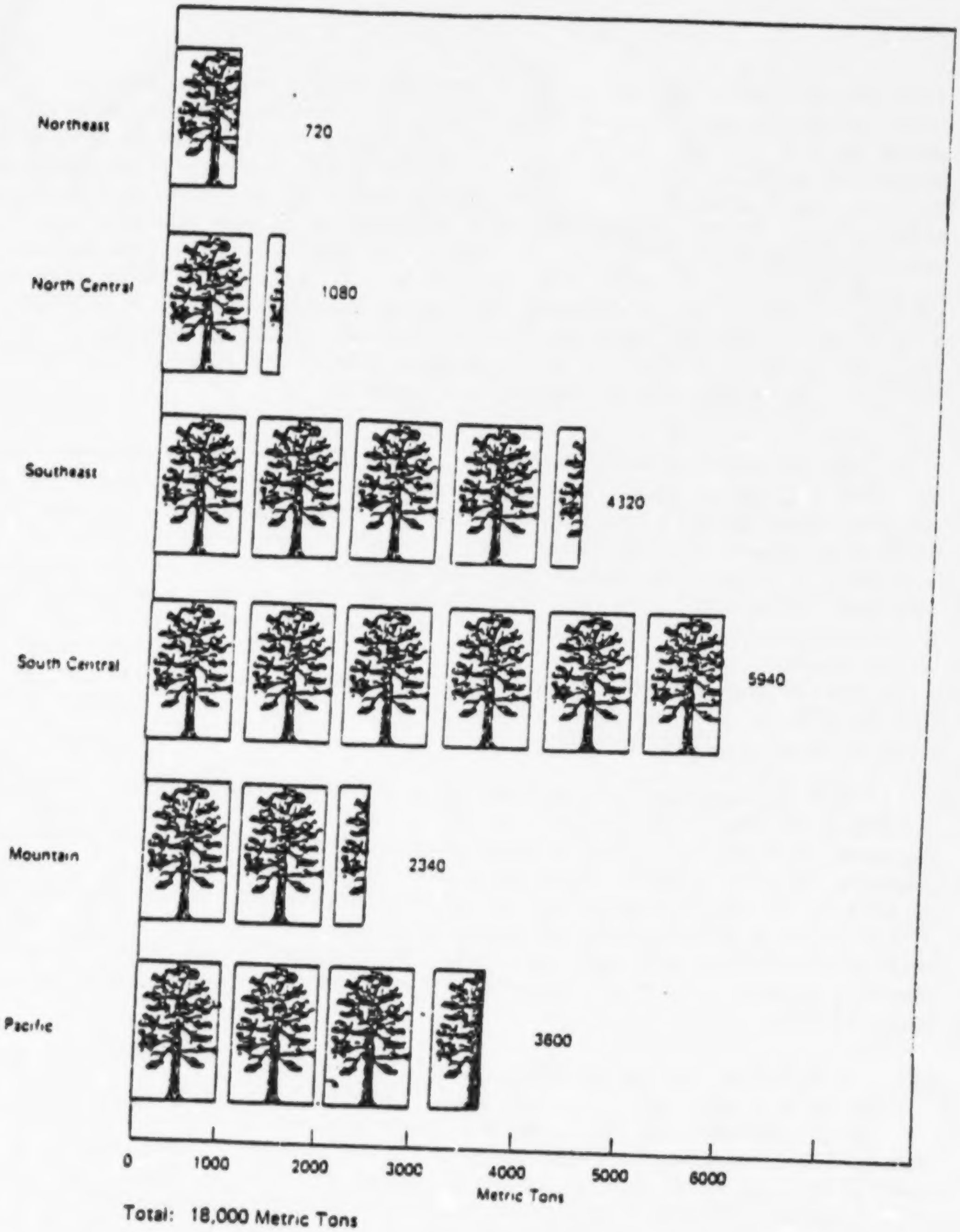


FIGURE 4-6. EXAMPLE OF REGIONAL DISTRIBUTION OF USE SOURCES--REGIONAL ESTIMATED CONSUMPTION OF PENTACHLOROPHENOL BY WOOD PRESERVATION PLANTS

Source: Scow et al. An exposure and risk assessment for pentachlorophenol. Final Draft Report. Contract EPA 68-01-3857. Washington, DC: Monitoring and Data Support Division, Office of Water Regulations and Standards, U.S. Environmental Protection Agency; 1980.

Following the application of PCP to wood at wood preserving plants, two important factors were identified and quantified: first, the end use of materials treated with PCP as illustrated in Figure 4-7; and second, the regional consumption of PCP-treated wood products as illustrated in Figure 4-8. Although it was not possible to combine these two factors in a verifiable manner (e.g., identify the number of fence posts in the North Central states), the end uses of an estimated 84.5% of pentachlorophenol produced in 1978 were identified. From this end use, it was estimated that 344 MT (or 1.9% of PCP used in preserving wood) are volatilized to the atmosphere based on the known properties of treated wood and PCP. It is also possible that PCP runs off the poles, fence posts and railroad ties when exposed to rainfall and contributes at nonpoint releases to groundwater, storm runoff basins, POTWs and surface streams. There were insufficient data available, however, to quantify this release.

Consumption of the remaining 15.5% of manufactured PCP is known, but associated releases are generally not as well understood. Production of sodium pentachlorophenol (NaPCP) is the second largest consumer, using 11.7% of annual PCP production. This is a relatively small segment of the chemical industry whose waste streams are not yet subject to Federal regulation. Consequently, insufficient data were available to estimate releases resulting from production of sodium pentachlorophenol. NaPCP is used to prevent bacteria growth in water towers, and in the textile and tanning industries with small associated environmental releases. It is also an additive to outdoor paints and is believed to be used in some toy paints manufactured and applied outside of the U.S. A major concern was identified with respect to NaPCP in paints in this materials balance, namely that misuse of outdoor paints, (i.e., indoors) and imported painted toys present a significant potential to human exposure. However, it was not possible to estimate the magnitude of these exposures.

4.5 SELECTED EXAMPLES FROM MATERIALS BALANCES FOR OTHER POLLUTANTS

Several components of various materials balance analyses are presented here as samples of methods typically utilized to estimate releases and as examples of special release situations. These selections are discussed in brief and, where appropriate, are accompanied by figures or tables.

4.5.1 Releases During Transportation

In the materials balance flow diagram (Figure 4-2) reference is made to the transport processes between major points in the pollutant's life cycle (extraction or synthesis, manufacture, storage, use and disposal) and subsequent pollutant releases associated with transportation. Relatively few standardized data are collected or maintained on potential environmental releases during transport largely due to wide variations in transport methods and handling practices by the carriers, themselves. In fact, documentation, when available, is usually limited

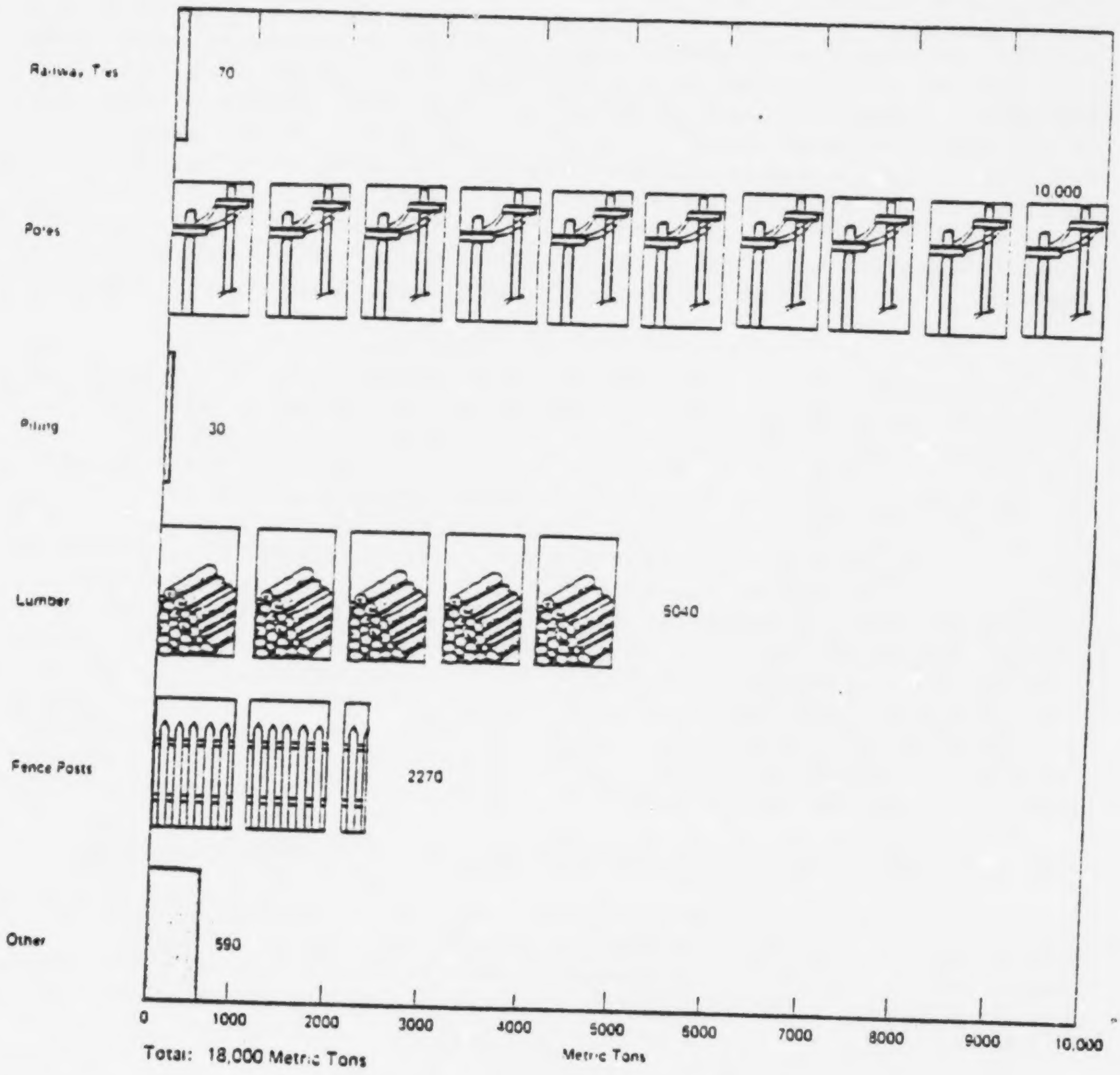
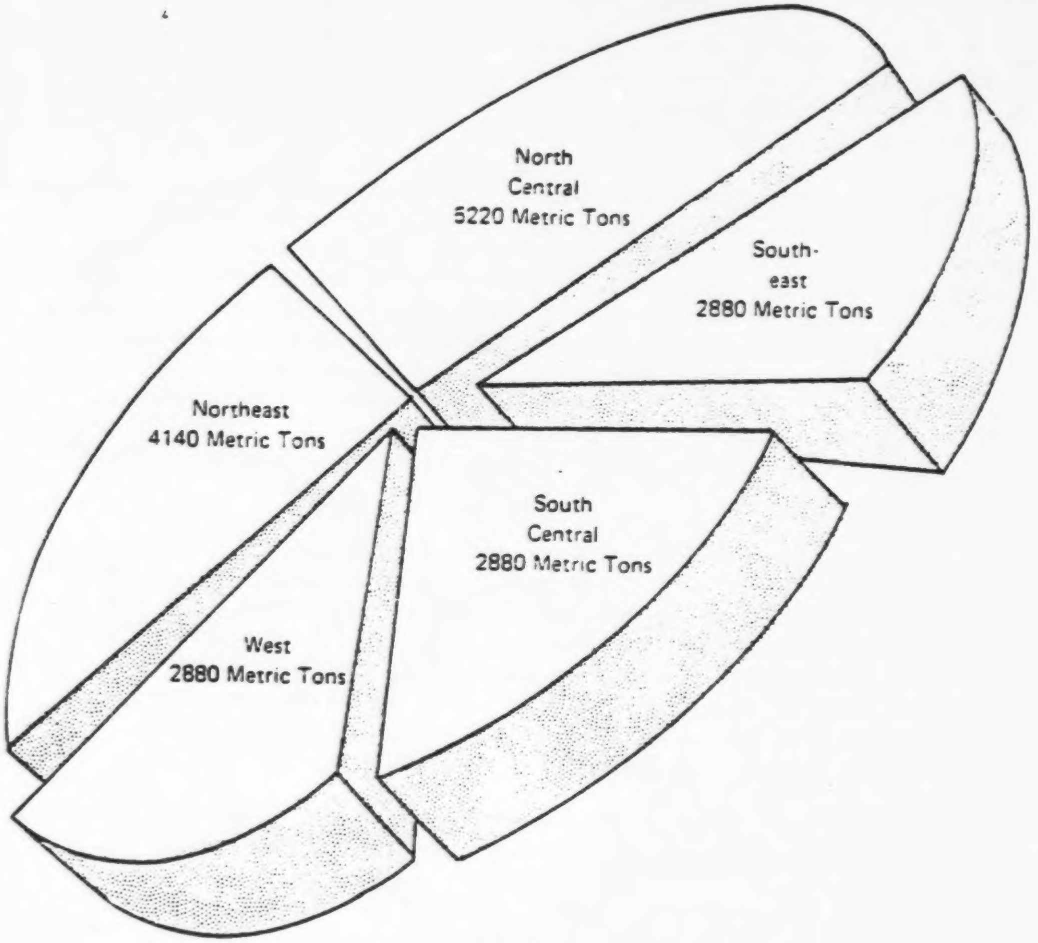


FIGURE 4-7 EXAMPLE OF END USE DATA--MATERIALS TREATED WITH PENTACHLOROPHENOL, 1978

Source: Scow, et al. An exposure and risk assessment for pentachlorophenol. Final Draft Report. Contract EPA 68-01-3857. Washington, DC: Monitoring and Data Support Division, Office of Water Regulations and Standards, U.S. Environmental Protection Agency; 1980.



Total: 18,000 Metric Tons

FIGURE 4-3 EXAMPLE OF REGIONAL CONSUMPTION DATA--U.S. REGIONAL CONSUMPTION OF WOOD TREATED WITH PENTACHLOROPHENOL, 1978

Source: Scow, et al. An exposure and risk assessment for pentachlorophenol. Final Draft Report. Contract EPA 68-01-3857. Washington. DC: Monitoring and Data Support Division, Office of Water Regulations and Standards, U.S. Environmental Protection Agency: 1980.

to reported occurrences of accidental spills or leaks. One estimation method is based on knowledge of the pollutant's principal transportation mode and of the types of its secondary users (large or small, nature of the operation).

In a materials balance for phthalate esters (Perwak et al. 1981a), it was reported that the chemicals were transported principally in liquid form via unpressured rail tank car, motor tank car, and, to a lesser extent, in small quantities (55 gallon drums).

The amount of loss associated with transportation (other than from accidents) was assumed to be a function of the size of the shipping container and the remaining amount after the container is "empty." Most esters are shipped by rail tank cars or tank trucks to distribution points and sites of major users. Some of the smaller operators among the 8000 compounders of plastics probably receive the plasticizers in 55-gallon drums. Small operators using rotational molding, coating processes, and small injection molding processes could possibly obtain a major portion of their plasticizer in this manner. Products made with these processes account for approximately 75,000 kkg of phthalate esters per year.

If it is assumed that 80% of this production is accounted for by 20% of the companies who are large enough to purchase in tank car lots, then the remaining 20%, or 15,000 kkg, might be delivered from the manufacturer to the compounder in 55-gallon drums. If between one cup and one quart of plasticizer remains in each empty drum, then between 0.11% and 0.46% or between 18 kkg and 68 kkg could be wasted and released to the environment when the drum is reconditioned, destroyed, or stored in a manner that allows the remainder to be released.

Though it is unknown what percentage of the phthalate transported in tank cars or tank trucks remains after the material has been delivered and the tank is "empty," an estimate of approximately one-tenth of one percent remaining was considered reasonable. This amount will either be cleaned from the tank prior to loading another commodity or will remain in the tank if the vehicle is in dedicated service. Information on numbers of tank cars that are dedicated is unavailable. For estimating purposes, it was assumed that 0.1% of the material transported is cleaned and flushed with water. The amount being transported in tank cars and tank trucks would be approximately 97% of the total production. A weighted average of the waste from the 3% delivered in 55-gallon drums and the 97% delivered in tank cars is still approximately 0.1%. For calculating a materials balance, it was assumed that 0.1% is lost because of transportation-related causes.

4.5.2 Publicly Owned Treatment Works

For some pollutants, discharge from publicly owned treatment works (POTWs) constitutes one of the largest direct releases to surface waters. Monitoring data on flow rates and pollutant concentrations for

POTW influents and effluents and on plant efficiency levels have been complied by the U.S. EPA Effluent Guidelines Division and U.S. EPA contractors. Considerable variability exists among these data sources. Some report on a single POTW and others report on groups; reporting methods and geographic coverage differs, also. Therefore, for materials balance analyses of different pollutants, POTW discharges have been estimated in several manners using the available data.

The discharge of cyanide from POTWs was estimated by three methods (Fiksel et al. 1981), all based on data compiled from sampling and analysis at 20 POTWs. One estimation was based on the average effluent cyanide concentration (210 μg/l) times the total effluent flow rate of all POTWs in the U.S. (34,000 MGD), resulting in an estimated cyanide discharge of 9800 MT/year. This approach assumes that the effluent concentrations at the 20 plants surveyed were representative of all plants across the country. An alternate approach used the total cyanide discharged from the 20 plants (169 MT/year) and the fact that the historical flow rates of these plants represent 2.7% of total U.S. POTW effluent flow to estimate a total discharge of 6300 MT/yr. This approach is probably the most accurate if the 20 plants are representative of all plants on a flow capacity basis. Finally, the percent removal of cyanide in the 20 plants was approximately 15%. Then for the total influent to POTWs of 18405 kkg/yr, the resultant discharge of cyanide would be 6400 kkg/yr. Each method assumes that the 20 plants surveyed are representative of all U.S. POTWs (Fiksel et al. 1981).

Another method was utilized to estimate the total zinc discharged from POTW to surface waters (Perwak et al. 1980c). A U.S. EPA contractor determined that POTWs meeting secondary treatment standards removed an average of 72% (range 45% to 96%) of the zinc in the influent. This conclusion was drawn from data on 22 of the 103 plants which operated to these standards and had sufficient data on all parameters of interest to allow analysis. The flow-weighted mean of the removal efficiencies was 81% for the 22 plants. Data were presented on removal efficiency for 10 primary treatment facilities in addition to the 22 secondary plants. The median value of removal efficiency for the primary plants was 39% while the flow-weighted mean was 17%. The latter was used in calculations to estimate partitioning between sludge and release to the aquatic environment.

Few data were available on improved metals removal during advanced treatment. However, it was assumed that metal removal efficiency is correlated to solids removal, and published data from a government survey were used to characterize metals removal efficiency in advanced secondary and tertiary treatment plants. Based on this survey, 28% of the total flow from POTWs undergoes primary treatment, 39% secondary, 18% advanced secondary, and 14% tertiary treatment. Advanced secondary is assumed to remove 88% of zinc, while tertiary treatment is assumed to remove 86%.

Table 4-6 summarizes the POTW zinc budget based on these assumptions and shows a total loading to POTWs of 22,083 MT, of which 7814 MT of zinc is discharged by POTWs to the aquatic environment, while 14,269 MT is discharged to land (Perwak et al. 1980c).

4.5.3 Natural and Inadvertent Releases

There are several sources of natural inadvertent releases of pollutants that contribute potentially large but usually widely distributed releases to the environment. The metals occur as natural constituents of the earth's crust in soils and rock formations throughout the U.S. As soils and rocks are weathered and eroded, the natural metals and minerals are released to surface streams. Nickel concentrations in soils generally range from 5 mg/kg to 500 mg/kg; the concentration in U.S. soils averages 30 mg/kg (McNamara et al. 1981). Other sources indicate that nickel is found at average concentrations of 50 mg/kg in sedimentary rocks, shale, and carbonate rocks. The average annual total suspended load of nickel in the United States is estimated to be 3.6 billion MT, 25% of which enters the major streams. Assuming an average nickel concentration of 30 mg/kg in soil, approximately 27,000 MT of nickel is discharged to surface waters via this route (McNamara et al. 1981).

Urban runoff also can provide a major contribution of pollutants to POTWs and surface waters each year. Mercury has been found in urban runoff at levels of about 0.2-85 μg/l. The mean value for a residential area of 720 acres in Rochester, NY was found to be 18.1 μg/l. with the median value for the same set of 10 data points in the range 4-5 μg/l. A second study involving less intensive sampling of stormwater and combined sewer runoff in 11 cities across the U.S. (including Rochester, NY) revealed concentrations ranging from less than 0.2 μg/l to 0.6 μg/l. The mean and median values for this data set were both equal to 0.3 μg/l. (The mercury concentration reported for Rochester in this study was 0.25 μg/l.) Lacking further information, a range of 0.2-20 μg/l in urban runoff was used to show the possible magnitude of the source. Thus, for runoff volumes of 17.3×10^{12} l/yr and 3.6×10^{12} l/yr going to surface waters and POTWs, respectively, 3.5-350 kkg goes to surface waters and 0.8-80 kkg to POTWs each year (Perwak et al. 1981b).

4.5.4 Releases to the Atmosphere

Atmospheric releases of a pollutant can be significant and are a potential pathway to surface waters. Included among the releases to air that are commonly evaluated in a materials balance are releases from chemical production, processing or refining, releases as a result of consumptive use and release as a byproduct of indirectly related processes. Automobile exhausts provide a source of atmospheric emissions which is typically considered as an area source of release and poses a serious problem in areas with high traffic densities.

Cyanides are one group of pollutants that has been detected automobile exhausts (Fiksel et al. 1981). The average rate of hydrogen

TABLE 4-6. EXAMPLE OF MATERIALS BALANCE FOR PUBLICLY OWNED TREATMENT WORKS: ZINC

	Treated Flow (MGD)[(1)]	Zinc Loading to POTW (MT)[(1)(2)]	Treatment Removal Efficiency	POTW Discharge (MT)	
				To Sludge	To Water
Primary treatment	7,525	6,341	.17(3)	1,078	5,263
Secondary	10,137	8,543	.81(3)	6,920	1,623
Advanced secondary	4,731	3,987	.88(4)	3,509	478
Tertiary	3,812	3,212	.86(4)	2,762	450
Total	26,205	22,083	.65 (overall)	14,269	7,814

(1) EPA 1978 Needs Survey, FRD-2.

(2) $L(MT/yr) = flow (MGD) \times 610 (10^{-6} g/l) \times 3.785 (l/gal) \times 365 (day/yr) \times 10^{-6} (\frac{MT}{g}) = 0.8427 \times flow.$

(3) Flow-weighted mean value calculated from Sverdrup and Parcel Associates data, February 1977.

(4) Assume advanced treatment removes Zn proportionately to TSS--estimated from tables 17, 27, 31 of EPA 1978 Needs Survey, FRD-2.

Source: Perwak, J. et al. An exposure and risk assessment for zinc. Final Draft Report. Contract EPA 68-01-3857. Washington, DC: Monitoring and Data Support Division, Office of Water Regulations and Standards, U.S. Environmental Protection Agency; 1980.

cyanide emissions has been reported to be 12 mg/mile. A fleet composite emission factor was estimated for hydrocarbons in automobile exhaust: 8 g/mile in 1976. The resultant CN/HC emission ratio (1.5 x 10^{-3}) multiplied by the total annual hydrocarbon emissions of 12 x 10^{6} kkg/year yields an estimate of HCN emissions of 18,000 kkg/year. Applying the CN/HC emission ratio to estimates of exhaust emissions compiled by U.S. EPA, the largest cyanide emissions from automobile exhausts would occur in areas of the highest traffic density, such as California (1500 kkg CN/year) or the combined states of New York and New Jersey (1500 kkg tons CN/year) (Fiksel et al. 1981).

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Scow, K.; Goyer, M.; Perwak, J.; Payne, E.; Thomas, R.; Wallace, D.; Walker, P.; Wood, M. An exposure and risk assessment for pentachlorophenol. Final Draft Report. Contract EPA 68-01-3857. Washington, DC: Monitoring and Data Support Division, Office of Water Regulations and Standards, U.S. Environmental Protection Agency; 1980.

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5.0 ENVIRONMENTAL PATHWAYS AND FATE ANALYSIS

5.1 INTRODUCTION

The results of the materials balance analysis will normally provide important information on pollutants that enter the environment; the amounts, types, forms, rates, and locations (both in terms of region and specific receiving medium) of environmental releases; and indications of direct exposure routes associated with the release of pollutants to the environment. If the environment and chemicals were static, materials balances, combined with information on receptor distribution, could be used to estimate exposure of humans and other biota to environmental pollutants. In most cases, the environment is not static but is dynamic in the sense that pollutants may be transported, undergo physical, biological and chemical transformations, accumulate or disappear, resulting in an environmental distribution quite different from that associated with the initial environmental release. For example, Figure 5-1 summarizes the major environmental transformations and transfers of trichloroethylene and illustrates the dynamic nature of the chemical's behavior following its release into environmental media (Thomas et al. 1981). Therefore, the environmental pathways and fate processes of the pollutant must be considered before one can determine with a reasonable degree of confidence the pollutant's chemical form and environmental concentrations to which receptors might be exposed.

In analyzing environmental pathways and fate, the following types of questions are important:

- Do the pollutants remain in the environmental media (air, water, land, biota) in which they are initially released or are there intermedia transfers?
- By what mechanisms are the environmental concentrations of the pollutant decreased or increased, e.g., biodegradation or intra- and intermedia transfer?
- What are the controlling external influences on intermedia and intramedia transfer?
- What are the rates of these transfers or reaction mechanisms?
- Are there any potential degradation products of concern with respect to environmental or health risks?
- Is a steady state pollutant concentration distribution in the environment achieved? Is the total environmental load increasing or decreasing? What are the environmental dynamics?

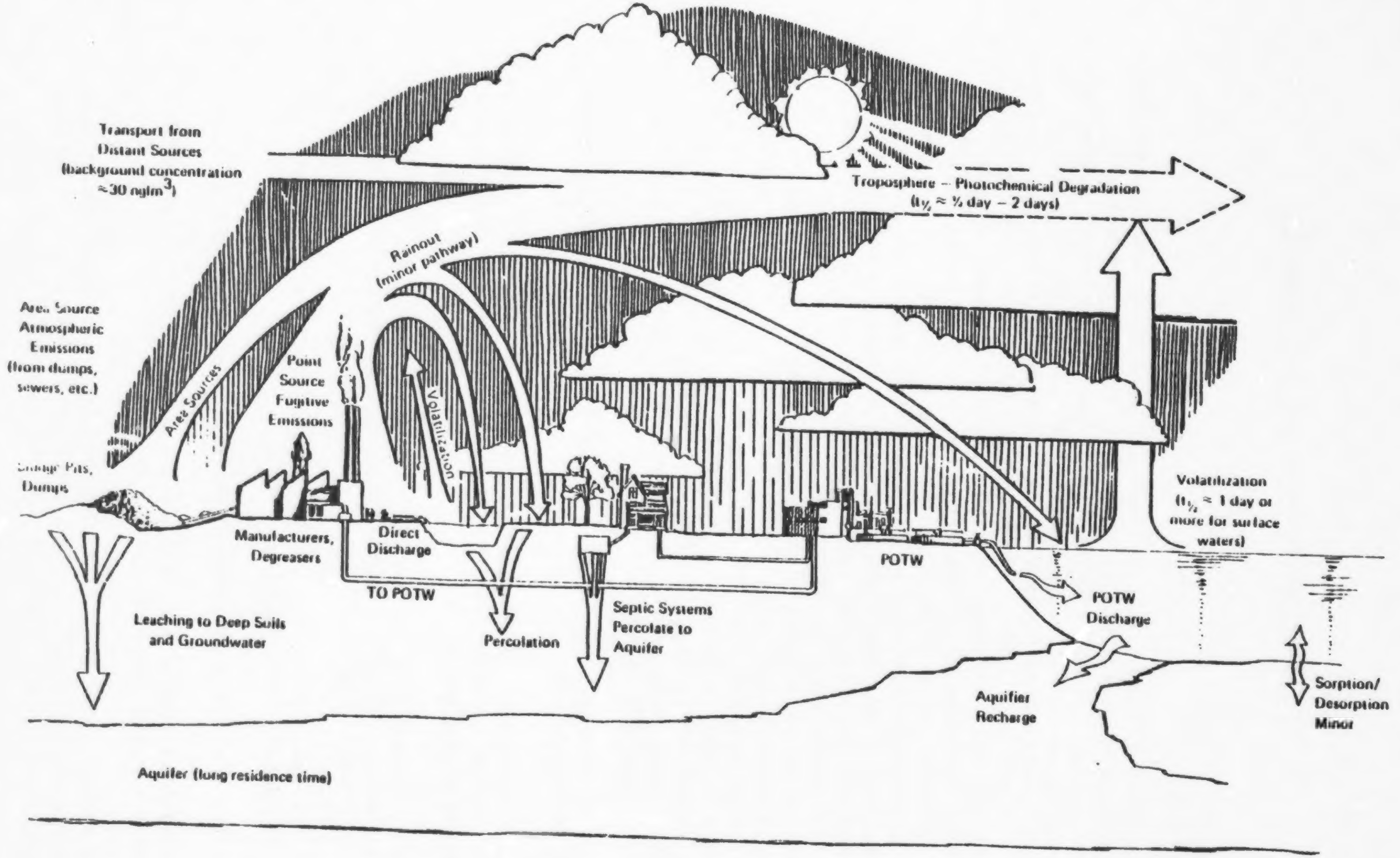
Transport from
Distant Sources
(background concentration
≈30 ng/m3)
Troposphere – Photochemical Degradation
(t½ ≈ ½ day – 2 days)
Area Source
Atmospheric
Emissions
(from dumps,
sewers, etc.)
Area Sources
Rainout
(minor pathway)
Point
Source
Fugitive
Emissions
Volatilization
Sludge Pits,
Dumps
Manufacturers,
Degreasers
Direct
Discharge
TO POTW
POTW
Volatilization
(t½ ≈ 1 day or
more for surface
waters)
Leaching to Deep Soils
and Groundwater
Percolation
Septic Systems
Percolate to
Aquifer
POTW
Discharge
Aquifier
Recharge
Sorption/
Desorption
Minor
Aquifer (long residence time)

FIGURE 5-1 EXAMPLE OF ENVIRONMENTAL PATHWAYS AND FATE ANALYSIS--MAJOR PATHWAYS OF TRICHLOROETHYLENE

Source: Thomas, R., et al. An exposure and risk assessment for trichloroethylene. Final Draft Report. Contract EPA 68-01-5949. Washington, DC: Monitoring and Data Support Division, Office of Water Regulations and Standards, U.S. Environmental Protection Agency; 1981.

- What is the anticipated spatial and temporal distribution of the pollutant: in the environment, in different media, among different types or forms of the pollutant, for different geographical areas, for different time frames? Are these distributions confirmed by monitoring data?

Answers to these types of questions will provide information on the exposure of different receptors that come in contact with various environmental media, particularly if these receptors play a role in the transport, reaction or distribution of the pollutant (e.g., biodegradation, uptake by plants, etc.) or are associated with a particular medium that accumulates the pollutant (e.g., persons who ingest contaminated fish tissue).

Monitoring data have often been considered as a substitute for environmental pathways and fate analysis since monitoring data directly provide the environmental distribution of pollutants. Ideally, an environmental pathway and fate analysis should be conducted in addition to review of monitoring data for several reasons:

(1) For many pollutants, particularly organic and new chemicals, monitoring data are limited, sporadic, and/or of questionable reliability.

(2) Analysis of available monitoring data does not enable the estimation of environmental concentration distributions in media or geographic locations for which monitoring data are not available.

(3) Analysis of monitoring data does not provide information on how and where physical, chemical and biological processes influence the environmental distribution of a pollutant.

(4) Analysis of the effects of different pollutant control options requires some knowledge of the relationship between environmental loadings and concentration distributions; this information is provided by fate models rather than by monitoring data.

Monitoring data, when available, can be a direct source of information for exposure analysis and can be used to calibrate (or extrapolate from) models used to estimate environmental distributions. However, in most exposure analyses, it will be important to evaluate pathways and fate data as well as aid in exposure determinations and in the development of regulatory recommendations.

5.2 GOALS OF ENVIRONMENTAL PATHWAY AND FATE ANALYSIS

The overall goal of environmental pathway and fate analysis is to establish the distribution of pollutants--both spatially and temporally--in all environmental media. This general goal can be divided into a number of specific objectives as follows:

(1) Define environmental media or compartments of importance to the environmental behavior of the pollutant, including subcompartments such as soil layers, aerobic or anaerobic zones, where necessary.

(2) Identify important mechanisms for transport and physical, biological and chemical change (pathways) of the pollutant within and among environmental media.

(3) Summarize and/or develop data on the rates of these transfer and reaction processes, determine the processes that control environmental fate and distribution, and identify predominant chemical forms or degradation products in various media.

(4) Estimate "lifetimes" or half-lives of pollutants in the environment

(5) Using materials balance/environmental loading estimates as inputs, trace the environmental pathways of pollutants from their sources to their sinks or ultimate distribution in the environment.

(6) Estimate average or representative pollutant concentrations and their time dependence in specific environmental media.

(7) Estimate concentrations and their time dependence in specific geographical locations--e.g., river basins, streams, rain, air sheds, etc.

(8) Use monitoring data to compare (and to improve) the results of environmental pathways and fate analysis wherever possible.

(9) Using pathways and environmental fate analysis, develop information for use in exposure analysis, and provide a basis for estimating quantitative relationships between environmental releases and exposure.

Ideally, a pathways and fate analysis traces all of the environmental releases of pollutants from specific sources through the environmental pathways that occur, and combines the resultant contributions of each release and transfer to obtain the spatial and temporal distribution of the pollutant in the environment. A careful accounting of pollutant inputs, inter- and intramedia transfers, and transformation/accumulation/degradation processes, should reveal the variation in distribution of the pollutant over time. This might be accomplished by using a simple partitioning model for a rough estimate, a complex environmental model or similar analytical techniques. Large-scale multimedia models exist; however, they have been designed either for specific pollutants or for specific environmental compartments and geographical areas. These large models require extensive and elaborate calibration procedures. Furthermore, the set of necessary input data--loading rates, transport and transformation rates, and other characteristics of the pollutant--is difficult to obtain or the data are not reliable enough for the results to be credible. Resource allocations further constrain such efforts. As a matter of necessity, environmental fate and pathway analyses often are fragmentary and incomplete, focus on only a few major pathways, and do not give complete distributions of concentrations of the pollutant. To be useful in exposure analyses, environmental fate and pathways analysis should at a minimum:

- distinguish key pathways from insignificant ones;
- focus on key pathways and on media where the amount or concentration of pollutant is large and where exposure of humans and other biota is expected;
- estimate a probable range of pollutant concentrations in different environmental media, with time and space resolution appropriate to pollutant sources and receptor exposures of concern;
- provide estimates of uncertainties that can be carried through the exposure or risk analysis.

The outputs of the pathways and fate analysis will be greatly constrained by the amount of information available concerning the physical, chemical, and biological characteristics of the pollutant; the types, nature, and location of the pollutant sources; the existence of models or calculational approaches available to estimate the concentrations; and the resources committed to the analysis.

In keeping with the goals of exposure and risk assessments within the Office of Water Regulations and Standards, the methodology focuses on water-related pathways and fate analysis. Non-water-related pathways should, of course, be considered because of the interrelations among environmental media, and in order to obtain a perspective on total exposure.

5.3 ENVIRONMENTAL PATHWAY AND FATE ANALYSIS METHODS

Three general methods useful for environmental pathway and fate analysis are described in this section. The methods have similar goals, several common steps, and may use some of the same data and information. Each one, however, has a different focus. The choice of approach will depend upon the nature of the pollutant, the scope of the exposure analysis, and the availability of data. In general, portions of more than one approach may be used and the results integrated in order to develop a more complete understanding of the environmental pathways and fate of a pollutant.

5.3.1 Environmental Scenario/Case Example Method

This approach will provide a qualitative assessment of pathways and fate mechanisms, supplemented by semi-quantitative information on pollutant distribution where sufficient depth of analysis of specific case examples is gained from literature sources. It begins with a brief review of materials balance and environmental loading data to identify relevant scenarios or case examples for a particular pollutant (see Figure 5-2 for steps in process). Each major source category is identified and hypotheses are developed concerning pollutant fate, beginning with the source and proceeding to an ultimate sink or environmental distribution.

For example, considering agricultural application as a major source of a substance used as an herbicide, one would indicate diagrammatically the likely pathways and fate processes beginning with the application and including: soil adsorption/desorption, chemical decomposition, biodegradation in the soil, volatilization, runoff and leaching into local waterways, uptake by plants or animals and distribution along the food chain (i.e., all major known fate mechanisms). Exposure routes suggested by this scenario include ingestion through food and drinking water (both humans and non-humans) and possibly skin absorption through contact with polluted water. A scenario such as this describes the likely pathways to be examined further or validated in subsequent steps.

The second step is to assemble and review available data to aid in evaluation of the pathway and distribution hypotheses. Literature data from both laboratory and field studies, as well as measured concentrations in the environment would be reviewed for mechanisms and rates of transport or chemical and biological transformation. Data on the physical, chemical, and biological characteristics relevant to determining the pollutant's fate in the environment would also be reviewed. Using herbicide application again as an example, one would review laboratory and field data on plant uptake, soil adsorption, concentrations found in soils and water, the rates of transfer from soils to ground (through leaching) or surface water (through runoff) or to air, as well as data on speciation, photolysis, biodegradation, hydrolysis, and other transformation processes. These data can provide quantification or at least support comparison of the processes or major pathways involved.

When no data are available, one of several estimation techniques may be used to provide a rough idea of the significance of particular properties of a chemical in its environmental fate. For example, Lyman et al. (1982) have compiled methods for estimating a number of physical, chemical and biological properties of organic chemicals in one handbook; these methods will be computerized in the near future.

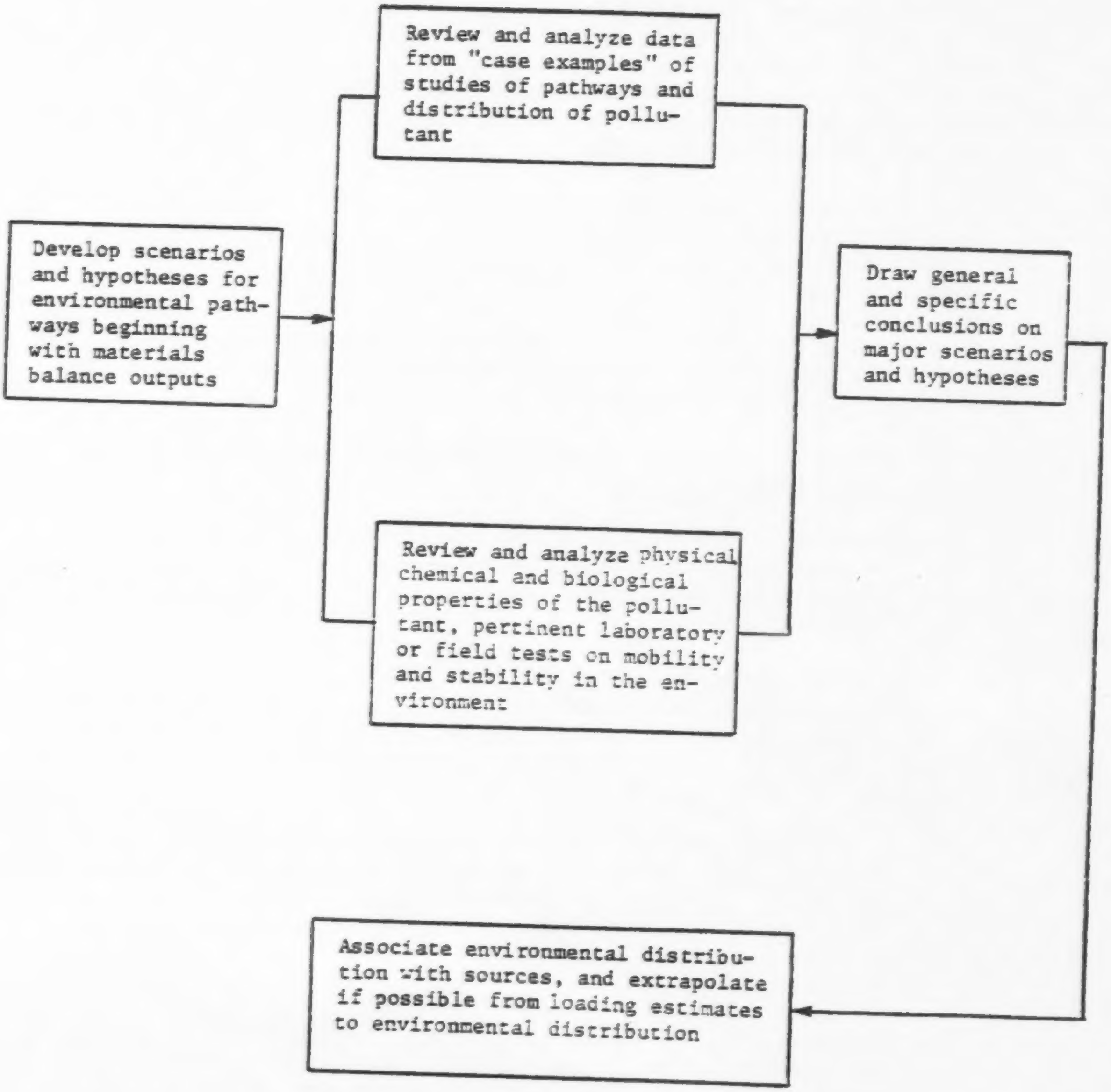
Develop scenarios and hypotheses for environmental pathways beginning with materials balance outputs
Review and analyze data from "case examples" of studies of pathways and distribution of pollutant
Review and analyze physical chemical and biological properties of the pollutant, pertinent laboratory or field tests on mobility and stability in the environment
Draw general and specific conclusions on major scenarios and hypotheses
Associate environmental distribution with sources, and extrapolate if possible from loading estimates to environmental distribution

FIGURE 5-2 DIAGRAM OF ENVIRONMENTAL SCENARIO APPROACH TO PATHWAYS AND FATE ANALYSIS

The third step is to draw both general and specific conclusions concerning the key factors influencing the fate of the pollutant, how the pollutant is partitioned in the environment, likely concentrations in each compartment, and so forth. General conclusions may indicate that certain sources are associated with higher water concentrations in a particular habitat than others, or that one transformation process is more important than others in the ultimate fate of a substance. Specific conclusions may be drawn from selected subjects described in the literature, and may yield either semi-quantitative relationships between loading rates and environmental concentrations, or specific data relating to the rates of typical processes.

The final step is to relate the specific sources and loadings given in the materials balance to the pollutant's environmental distribution. This step can indicate where likely exposure to the pollutant may occur and give some idea of how exposure may change as a function of future control strategies. In a sense, this final step involves reexamination of the scenarios developed in the beginning, attempting to quantify them and show the relationships between the sources and distribution of the pollutant and resultant exposure.

The environmental scenario method seems most appropriate in the following situations:

(1) Sources of the pollutant are relatively well known and major sources can be distinguished from minor ones in terms of the quantity released to the environment and its relationship to potential exposure.

(2) The pollutant is well-known in the sense that field and laboratory studies exist, data on the chemical, physical and biological characteristics of the pollutant are available, and the behavior of the pollutant in the environment has, at least, been addressed by others.

(3) Monitoring data for the pollutant are available, so that measured data rather than estimates can be used in forecasting exposure. The fate and pathway analysis in this case is more important for linking sources to environmental pathways and spatial and temporal distribution rather than to estimate concentrations.

(4) Large-scale models describing the pollutant pathways are either not available, not useful, overly complex, or too general or gross in scale for application given the resources available. Additionally, the availability of other data described above may make the use of complex estimation techniques unnecessary.

5.3.2 Critical Pathway/Distribution Estimation Method

This approach is focused on identifying the critical pollutant pathways that are most influential in determining distribution of the pollutant and the resultant concentrations in the environment. The steps involved are shown diagrammatically in Figure 5-3 and described briefly below.

This approach also begins with the results of the materials balance analysis. However, rather than scenarios of environmental pathways related to particular production or use patterns, aggregate loading rates (temporal or spatial combinations) for different media are first developed, either on a nationwide basis or for specific regions with identified environmental loading patterns. For example, the total annual loading from direct and indirect releases to air, water, soil, and occasionally biota, etc., are determined from the materials balance results; estimates are then made of the sizes of receiving media, e.g., volume of water, air or soil receiving the total loading. If possible, these estimates may be made for regional or other smaller scale geographical locations, to focus on areas of concern. General environmental characteristics of the receiving media important to the pollutant's distribution are also estimated--e.g., pH, soil moisture content, etc.

Second, data on the physical, chemical and biological characteristics of the pollutant are reviewed. Pertinent data may include molecular weight, aqueous solubility, vapor pressure, octanol/water partition coefficient, biodegradation rates, chemical reaction rates, etc. These data are used to provide insight into important transformation processes that remove the pollutant and/or convert it to other products or potential contaminants. Products identified may also be considered for toxicity and further transformation. (Time and resources generally prohibit full consideration of these products in an exposure assessment.)

Third, pathways and processes that result in transfer of the pollutant from one medium to another are evaluated in order to identify the critical transfer pathways and estimate the relative rates of the transfer processes. For example, for a pollutant initially released to water, vaporization and sedimentation might be considered in order to determine whether and how rapidly the pollutant is transferred to the air or soil media. Basically this analysis is a simple partitioning study, to determine if the pollutant tends to remain in the initial receiving medium or is transferred to others. In some cases, all of the pollutant may be rapidly redistributed to other media; while in others, a slowly established equilibrium distribution may be indicated.

Following an initial determination of the partitioning, the next step is a more detailed examination of the pollutant fate in the media that are of most interest, e.g., those media or subcompartments into which the pollutants are likely to be partitioned. Each major fate process is reviewed, using rate and equilibrium relationships and estimation techniques from the literature, pollutant specific data (e.g., rate constants) from laboratory or field studies, model ecosystem results, etc. Typical processes to be examined include:

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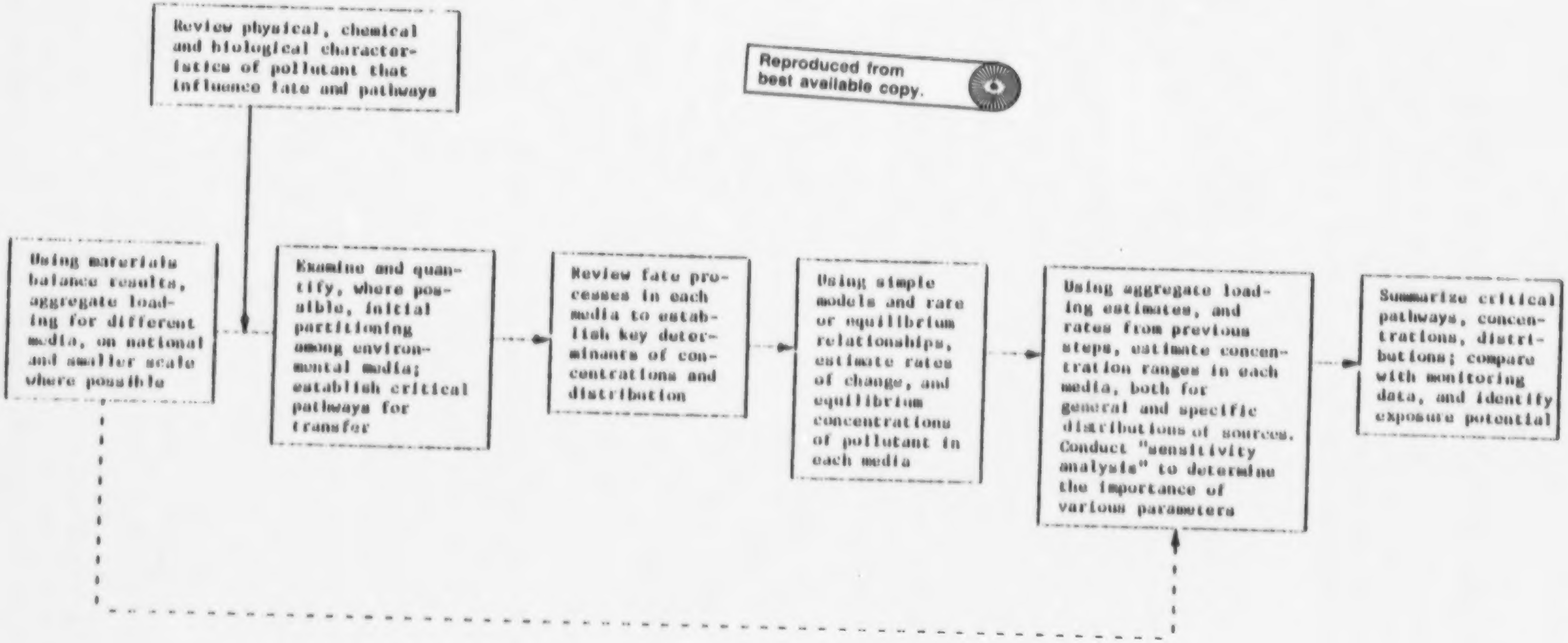

Review physical, chemical and biological characteristics of pollutant that influence fate and pathways
Using materials balance results, aggregate loading for different media, on national and smaller scale where possible
Examine and quantify, where possible, initial partitioning among environmental media; establish critical pathways for transfer
Review fate processes in each media to establish key determinants of concentrations and distribution
Using simple models and rate or equilibrium relationships, estimate rates of change, and equilibrium concentrations of pollutant in each media
Using aggregate loading estimates, and rates from previous steps, estimate concentration ranges in each media, both for general and specific distributions of sources. Conduct "sensitivity analysis" to determine the importance of various parameters
Summarize critical pathways, concentrations, distributions; compare with monitoring data, and identify exposure potential

FIGURE 5-3 DIAGRAM OF CRITICAL PATHWAY/DISTRIBUTION ESTIMATION METHOD FOR ENVIRONMENTAL PATHWAYS AND FATE ANALYSIS

Air	free radical oxidation, photolysis, adsorption to aerosols, dry deposition, fallout, rainout, scavenging
Water	hydrolysis, photolysis, chemical oxidation, precipitation, adsorption/desorption with sediments, volatilization, biodegradation
Soil	leaching, hydrolysis, surface photolysis, chemical oxidation, volatilization, uptake, adsorption, complexation
Biota	biodegradation, metabolism, bioaccumulation, biomagnification, etc.

Some of these processes may have been considered earlier, since they are ones that result in intermedia transfer. By using very simple models, generalized rate equations, or measured values reported in the literature, the rates of degradation or transfer within media can be estimated. Those processes are identified that are major determinants of the rate of transfer, decomposition, or reaction, and hence the ambient concentration levels.

The next step is to utilize the aggregate loading rates, general partitioning estimates, and the estimated transfer or reaction rates to calculate likely ranges of concentration of the pollutant in the environmental media. Frequently, these calculations will involve "single compartment" models or equations along with physical/chemical properties. One would assume that the entire loading of the pollutant enters one medium with a specific volume, and estimate the resultant concentrations of pollutant, changes over time, and/or steady-state concentrations. Steady-state values will be important for highly persistent pollutants; transformation and transfer rates control the concentration distribution of pollutants that are more mobile or shorter-lived in the environment. In some cases, several environmental compartments (and/or decay processes) will have to be considered simultaneously, where both are important. "Feedback" from one set of calculations to another is required. In general, however, these estimates are made to place boundaries on the distribution and concentration of the pollutant and not to determine absolute values. Thus, use of more complex, multi-compartment or single compartment models may not be necessary or appropriate for this approach.

Estimates of environmental concentration ranges can then be made for smaller geographical locations, using specific source loadings and parameters describing the associated receiving media. A number of simple models are available for this approach, for example, Mackay's fugacity model (Mackay 1979) and simple computer models such as PLUME (EPA 1979), among others. These models are described in greater detail in Section 5.3.3. Sensitivity analysis can be conducted to determine which parameters influence the outcome to the greatest extent.

The final step in this approach is to summarize the results in terms of the critical pathways, estimates of the environmental distribution and pollutant concentration ranges, and comparison of these concentration ranges with available monitoring data.

This overall method is appropriate for considerations in several situations:

(1) when the pollutant is not well-known and few laboratory or field environmental data are available;

(2) where there are only a few types of important pollutant sources, and where distributions can be easily estimated, or where data exist on major releases in specific areas;

(3) where monitoring data are sparse, or are widely distributed or uncorrelated with release patterns;

(4) where insufficient data and resources are available to use more complex environmental models, or where the quality of input data does not justify their use;

(5) in specific situations identified by using the environmental scenario method.

5.3.3 Modeling Approaches

As indicated earlier, simple calculations and modeling approaches are an integral part of the environmental scenario and critical pathway/distribution estimation methods. However, these simple models usually do not account for intermedia transfers and equilibrium relationships between different media. Multimedia modeling may be warranted, resources permitting, if sufficient data exist on the chemical, physical and biological characteristics of the pollutant, if accurate source and loading data are available, and if appropriate models are available. The results of such models can provide a more accurate estimated distribution of the pollutant in the environment and provide a useful mechanism for estimating the effects of different regulatory approaches. Once the models have been validated and calibrated, they can be used in many situations with modest resource commitments.

The general steps to be followed in multimedia modeling approaches are:

(1) Identify, from materials balance results, the major pollutant sources and geographical areas considered for modeling.

(2) Identify the most significant environmental pathway for the pollutant under the conditions selected above.

(3) Select the individual models or multimedia model applicable to the situation, i.e., type of emitting source, pollutant, receiving media.

(4) Compile the input data required by the model(s) selected, e.g., source/loading data, pollutant characteristics and properties, environmental characteristics, and time.

(5) Use the model(s) to estimate pollutant fate (transport, transformation, concentration) in the different media.

(6) Compare the model results to the results of the two approaches described above, and to monitoring data. Comparison with monitoring data is frequently required for calibrating the model, and should be carefully accomplished before the model is used for predictions.

(7) Perform a sensitivity analysis of model parameters that are uncertain, or vary significantly in different locations.

(8) Analyze modeling results for insight into exposure of various species, effects of regulatory actions, impact of reduction in loading rates on environmental levels, significance of environmental process in determining pollutant fate, etc.

A number of computer models have been sponsored by the U.S. Environmental Protection Agency and other agencies to aid in pollutant environmental fate and exposure assessments. Information about specific models is not reiterated in this report; instead, the reader is referred directly to EPA's Environmental Modeling Catalogue (U.S. EPA 1979) for detailed information on available models. Other model reviews include Miller (1978), among others.

Some examples of available models considering a single environmental medium include the EPA UNAMAP system (air), EXAMS (surface water). EXPLORE (stream), ARM (watershed) and SESOIL (soil). Examples of multimedia models that link two or more environmental media include UTM and ALWAS (air to watershed/stream), CMRA (overland to stream), and TOHM (air to watershed/water). Other models include Mackay's fugacity method, which estimates equilibrium partitioning of a pollutant between air, water, sediment and biota (Mackay 1979), and Neely's microcosm model (Neely 1978).

Most pollutants released to the environment are likely to be transferred between media. A model can provide a fairly detailed approach for tracing pollutant levels in different media when the substance is subject to removal or transformation by competing processes. By accounting for the net rate of pollutant transport or transformation, the model characterizes the pollutant's mass distribution in the environment, temporal and spatial. Sensitivity analysis enables determination of the significance of a particular process or variable. With an efficiently developed model or set of models, assuming input data are available, the modeling approach can provide valuable information, in a timely and cost-effective manner.

However, currently there are significant difficulties in applying multimedia models to most pollutants. Although a considerable amount of research has been done in this area, most of the multimedia models are still under development or have not been fully verified. Adequate data (either chemical or environment specific) for input to models are also often lacking. When the input data used are uncertain or must be estimated, the results lack precision. The unavailability of a suitable, verified model and/or sufficient input data precludes the use of multimedia models in many instances. When multimedia modeling is performed, results must be interpreted with care, because a selected model may exclude certain pathways related to the complete traverse of the substance through the environment. Since the results are obtained from environmental conditions, a scientist has to be concerned with the extrapolation of the conditions simulatued to generalized results and environments.

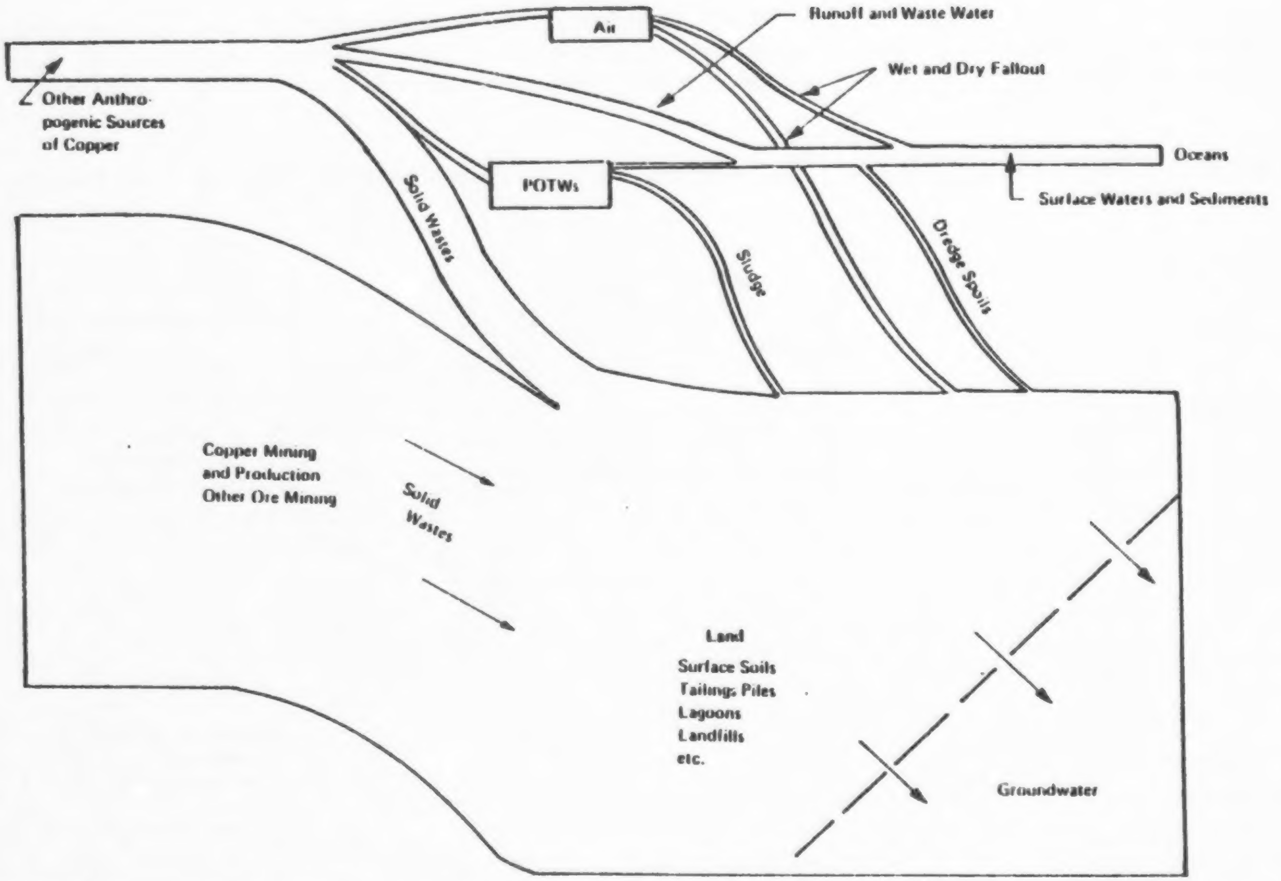
5.4 EXAMPLES OF ENVIRONMENTAL PATHWAYS AND FATE ANALYSIS

Several illustrative examples of the methods described earlier are presented in this section. Only portions of the calculations, results or discussions are given to indicate the types and results of the apprcaches.

5.4.1 Environmental Scenario Method

In an exposure and risk assessment for copper (Perwak *et al*. 1980) the environmental scenario method was used to link sources and pathways with environmental distribution. This method was selected for this pollutant because sufficient monitoring data were available for estimating exposure, and field and laboratory studies had documented the physical, chemical and biological processes that determine the pollutant's behavior in the environment. Figure 5-4 depicts the major environmental pathways for copper released to the environment through human activities.

Figure 5-5 shows in greater detail environmental scenarios for several of the environmental pathways of copper. In the second scenario, wastes from primary copper production, coal mining, and copper ore mining and benefication are shown to enter the air and water environment by several paths; runoff and leaching mechanisms carry wastes to surface water or ground water, respectively. The surface water/sediment interaction and other flows are also shown. In the fifth scenario, several uses of copper are


Air
Runoff and Waste Water
Wet and Dry Fallout
Other Anthropogenic Sources of Copper
Oceans
Surface Waters and Sediments
POTWs
Solid Wastes
Sludge
Dredge Spoils
Copper Mining
and Production
Other Ore Mining
Solid Wastes
Land
Surface Soils
Tailings Piles
Lagoons
Landfills
etc.
Groundwater

Note: Quantities of copper moving in each pathway are roughly proportional to the thickness of each pathway shown. Slow movement from groundwaters to surface waters not shown.

FIGURE 5-4 EXAMPLE OF ENVIRONMENTAL SCENARIO IDENTIFICATION--SCHEMATIC DIAGRAM OF MAJOR PATHWAYS OF COPPER RELEASED TO THE ENVIRONMENT BY HUMAN ACTIVITIES

Source: Perwak, J. et al. An exposure and risk assessment for copper. Final Draft Report. Contract EPA 68-01-3857. Washington, DC: Monitoring and Data Support Division, Office of Water Regulations and Standards, U.S. Environmental Protection Agency; 1980.

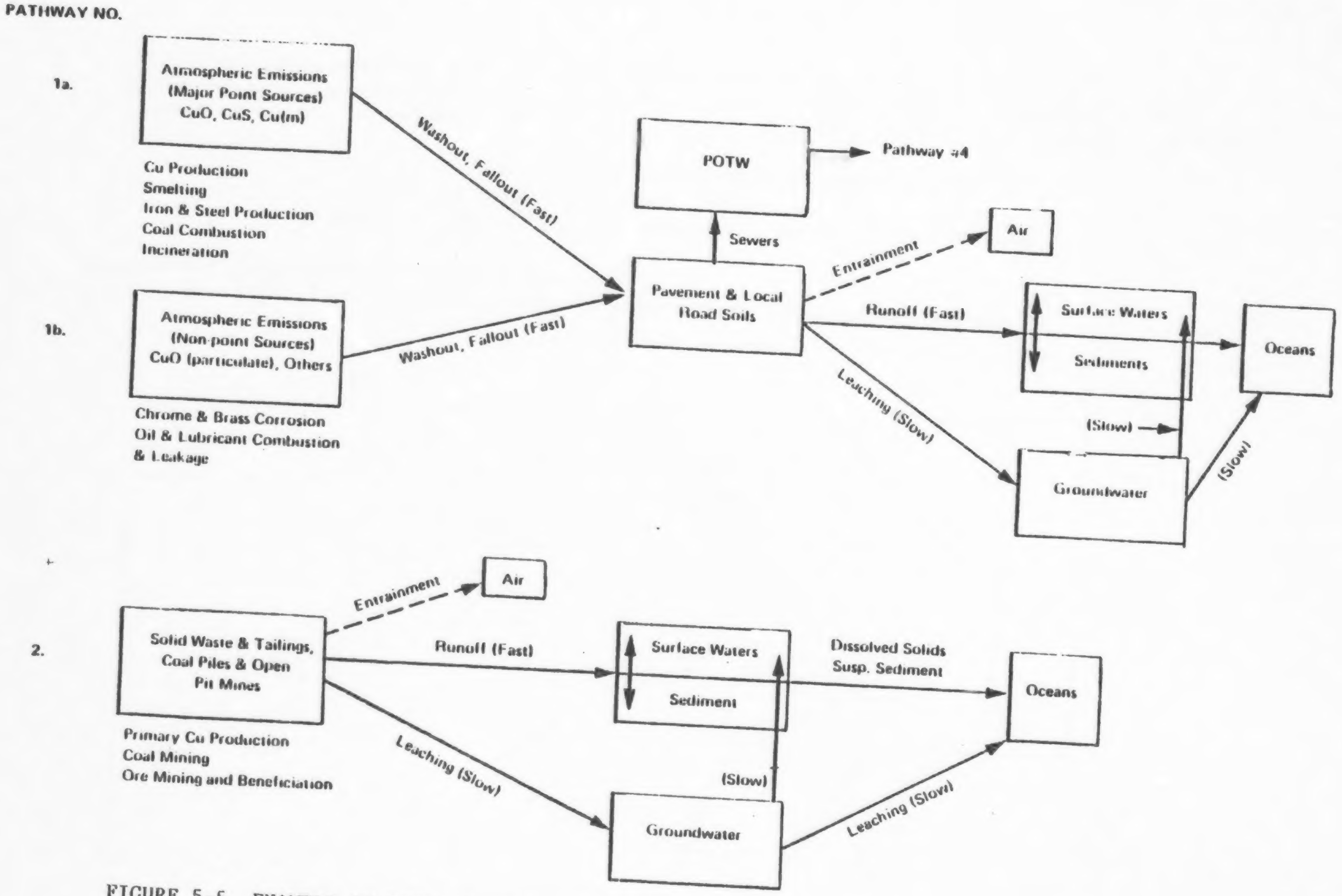

PATHWAY NO.
1a.
Atmospheric Emissions (Major Point Sources) CuO, CuS, Cu(m)
Cu Production
Smelting
Iron & Steel Production
Coal Combustion
Incineration
Washout, Fallout (Fast)
1b.
Atmospheric Emissions (Non-point Sources) CuO (particulate), Others
Chrome & Brass Corrosion
Oil & Lubricant Combustion & Leakage
Washout, Fallout (Fast)
POTW
Pathway #4
Sewers
Pavement & Local Road Soils
Entrainment
Air
Runoff (Fast)
Surface Waters
Sediments
Oceans
Leaching (Slow)
(Slow)
Groundwater
(Slow)
2.
Solid Waste & Tailings, Coal Piles & Open Pit Mines
Primary Cu Production
Coal Mining
Ore Mining and Beneficiation
Entrainment
Air
Runoff (Fast)
Surface Waters
Sediment
Dissolved Solids
Susp. Sediment
Oceans
Leaching (Slow)
(Slow)
Groundwater
Leaching (Slow)

FIGURE 5-5 EXAMPLE OF ENVIRONMENTAL SCENARIO ANALYSIS--TYPICAL ENVIRONMENTAL PATHWAYS OF COPPER

Source: Perwak, J. et al. An exposure and risk assessment for copper. Final Draft Report. Contract EPA 68-01-3857. Washington, DC: Monitoring and Data Support Division, Office of Water Regulations and Standards, U.S. Environmental Protection Agency; 1980.

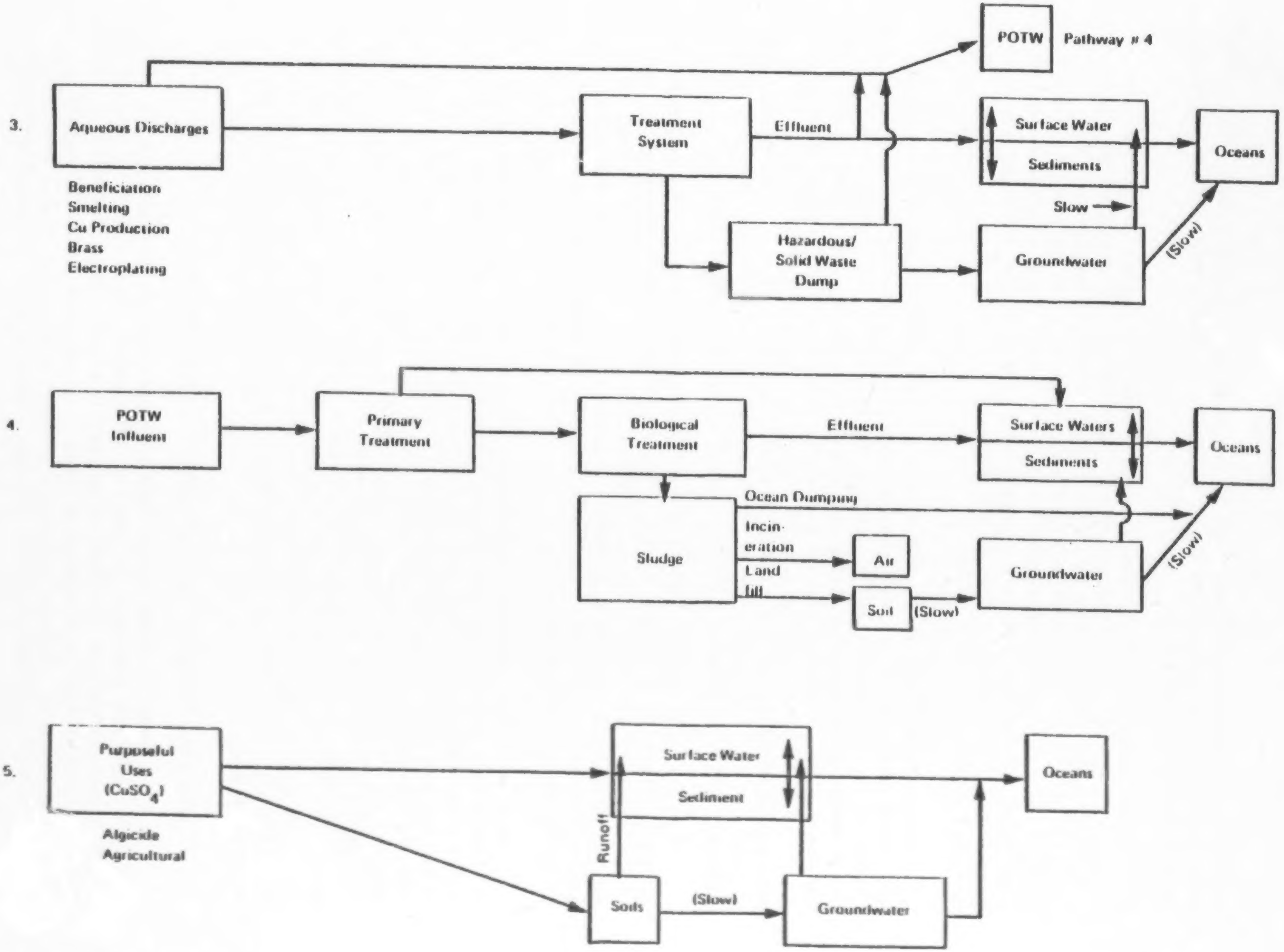

3.
Aqueous Discharges
Beneficiation
Smelting
Cu Production
Brass
Electroplating
Treatment System
Effluent
POTW
Pathway # 4
Surface Water
Sediments
Oceans
Slow
Hazardous/ Solid Waste Dump
Groundwater
(Slow)
4.
POTW Influent
Primary Treatment
Biological Treatment
Effluent
Surface Waters
Sediments
Oceans
Sludge
Ocean Dumping
Incin- eration
Air
Land fill
Soil
(Slow)
Groundwater
(Slow)
5.
Purposeful Uses ($CuSO_4$)
Algicide
Agricultural
Surface Water
Sediment
Runoff
Soils
(Slow)
Groundwater
Oceans

FIGURE 5-5 EXAMPLE OF ENVIRONMENTAL SCENARIO ANALYSIS--TYPICAL ENVIRONMENTAL PATHWAYS OF COPPER (Continued)

shown--as an algicide ($CuSO_4$) and as an agricultural chemical. The pathways from soil to ground and surface water, to sediments, and ultimately to the ocean are shown.

These general descriptions were the starting point for subsequent literature review, quantification of flow rates from selected sources, and ultimately analysis of concentrations in the environment. For example, in order to describe the first scenario, the nature of solid wastes and tailings was reviewed, along with data from studies of acid mine drainage, concentrations found downstream of mine drainage sites, incidents of groundwater contamination, and leaching studies from a variety of sites.

The analysis revealed that solid wastes, coal piles, and tailings are major sources of copper disposed of on land. Copper exposed as a result of mining practices is subject to greater translocation in the environment than releases from the other two sources due to the acid nature of the leachate. Surface streams draining mined areas have been shown to have localized spikes in copper concentration, with the level quickly decreasing as the stream recovers in pH and alkalinity values as a function of distance. The major processes affecting this reduction in copper concentration are dilution, sorption, and precipitation.

In municipal waste landfills the copper concentration in leachate is typically between 0.04-0.4 mg/l. Copper is quickly attentuated by the soil. Data on groundwater contamination were not available though such contamination is rare in a properly operated landfill. In old mined areas, acid mine drainage, and porous tailings enhance the possibility of groundwater contamination.

For the fifth scenario involving the agricultural use of copper sulfate, data describing the fate of copper in the soil, water and sediments were analyzed; field data were examined for indications of the roles of adsorption or sedimentation of copper and for mean and maximum concentrations in water or sediment. Use of copper sulfate as an algicide appears to be effective within a very short time frame, and field studies indicate that concentrations of copper ion in the water column decrease to background levels within a day following application. Copper is transferred from water to particulates, algae and sediments through sorption. Sediment core concentrations reflect the use of $CuSO_4$ over the years indicating that sediment is a significant ultimate reservoir for copper in aquatic systems.

5.4.2 Critical Pathway/Distribution Estimation Method

The Critical Pathway/Distribution Estimation Method was used in the pathways and fate analysis for pentachlorophenol (PCP) (Scow et al. 1980) which is characterized by limited monitoring data, adequate data on basic chemical properties, and a good general understanding of its overall materials balance. Little documentation was available on PCP emissions from particular consumers or producers. The critical pathways approach was used in a risk assessment of this pollutant in order to provide PCP concentration estimates in various media and to determine the critical pathways influencing its distribution. Since PCP use is concentrated in a few industry categories, the fate and pathways analysis was focused on these operations.

In order to provide a better understanding of the fate, distribution and potential for exposure to PCP following discharge from significant sources, simple quantitative models were used. Four sources to air were considered for their contribution to national atmospheric levels of PCP. Three sources--cooling towers, wood preserver evaporation ponds, and direct aquatic discharge as a general phenomenon--were considered for their local impact and exposure potential. The type of input data required included source characteristics (e.g., dimensions, emission or loading rate, etc.), environmental characteristics for a representative set of conditions (e.g., wind speed and direction) and chemical characteristics (e.g., transformation rates). As an example of how the approach is applied, the development of the equation describing local pollutant concentrations from a cooling tower plume is described briefly.

First, the assumptions made in developing the equations were defined. These assumptions included the values chosen for each variable, such as plume buoyancy and height, wind speed, temperature, and others. Also, variables not included in the equation but potentially influencing the resulting concentrations were identified (e.g., rainout, large-scale turbulence, chemical reactivity). Second, the fate of pentachlorophenol during cooling tower evaporation was characterized by a Gaussian concentration distribution using a simple plume model. The output of the model equation--PCP concentrations as a function of distance from the source for two plume source heights--were plotted, as in Figure 5-6. The results of the equation were used directly as concentrations from which to estimate human exposure in subpopulations residing within specified distances of a cooling tower.

5.4.3 Modeling Approaches

Computerized and hand-calculator models have been used in the environmental fate and pathways analysis of numerous priority pollutants. Three approaches applied in exposure and risk assessments for phthalate esters (Perwak et al. 1981) and dichlorobenzenes (Harris et al. 1981) are described below. (No example is given of the application of a complex multi-media model, though such models will undoubtedly prove to be useful in future exposures and risk assessments.)

5.4.3.1 Phthalate Esters

Based on two existing environmental fate models for phthalate esters: The Exposure Analysis Modeling System (EXAMS), developed by the U.S. EPA (Wolfe et al. 1979), and Neely's partitioning model (Neely 1978), ambient concentrations of di(2-ethylhexyl) phthalate (DEHB) were estimated in a simplified three compartment model for water (including sediment and fish). Some of the model's assumptions were adapted in this application to incorporate more current or relevant data developed

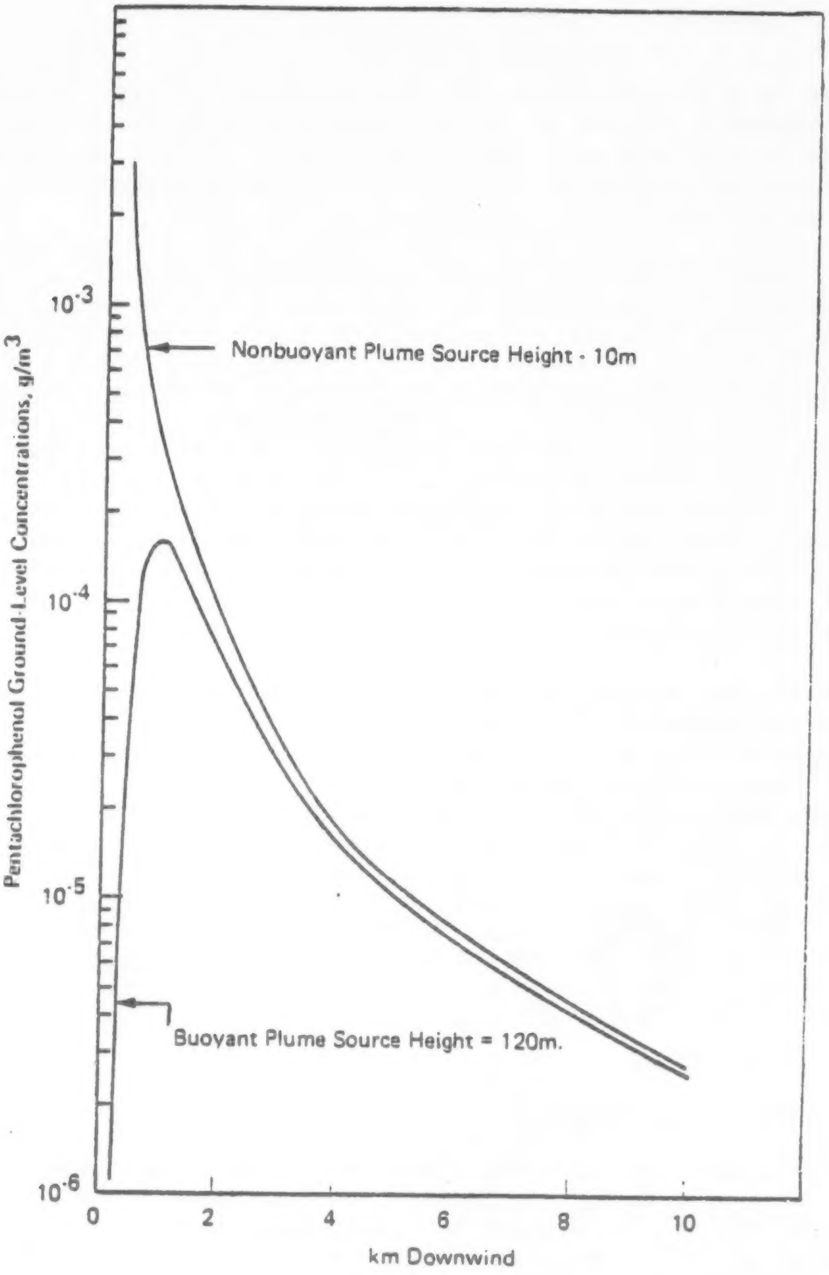


FIGURE 5-6 EXAMPLE OF USE OF SIMPLE QUANTITATIVE MODEL TO ESTIMATE ENVIRONMENTAL DISTRIBUTION--GROUND-LEVEL CONCENTRATIONS OF PENTACHLOROPHENOL IN THE PLUME DOWNWIND OF A COOLING TOWER (TWO SOURCE HEIGHTS)

Source: Scow, K. *et al*. An exposure and risk assessment for pentachlorophenol. Final Draft Report. EPA Contract 68-01-3857. Washington, DC: Monitoring and Data Support Division, Office of Water Regulations and Standards, U.S. Environmental Protection Agency: 1980 in the materials balance and in the review of physical and chemical properties. Some of the data were scaled for a national approach from a site-specific approach.

Concentrations in air in the U.S. were estimated using the equation:

$$\frac{dx}{dt} = \frac{Q}{H} - kx$$

where: x = mass concentration
t = time
Q = area source strength
H = mixing height
k = rate constant for removal.

The concentrations predicted by the models for DEHP in water, sediment, fish and air were then compared with measured concentrations reported in the literature. Figure 5-7 summarizes the predicted and measured levels. The results of this analysis indicated that DEHP is usually present at extremely low concentrations in air, and at low levels in water; it is subject to significant chemical transformation in air but virtually none in water; and it is likely to accumulate in sediment and fish to levels from two to three orders of magnitude greater than water column concentrations.

5.4.3.2 Dichlorobenzenes

For the environmental distribution analysis of 1,2-dichlorobenzene, two separate fate models were implemented and the results compared. Mackay's Level I fugacity approach was used assuming all environmental compartments--air, water, sediments, biota--were at equilibrium and connected and there was no degradation or transport out of the selected environment. The EXAMS model was run for three generalized, pre-compiled aquatic systems--a pond, an oligotrophic lake and a river. Input data to both models were based on materials balance information and physical/chemical properties of dichlorobenzene compiled from published literature.

For typical environmental loading rates, both models predicted a high sediment to water ratio (two to three orders of magnitude) under equilibrium conditions, and partitioning into biota. Table 5-1 summarizes the results. Table 5-2 gives more detailed results of the EXAMS model. Volatilization was the primary means of disposition from ponds and lakes, aquatic systems in which transport downstream is minimal. The differences in the results of the two models were due to the fact that a greater proportion of dichlorobenzene partitioned to the air compartment in the Mackay model and the fact that EXAMS considered kinetic processes, as well as simple partitioning.

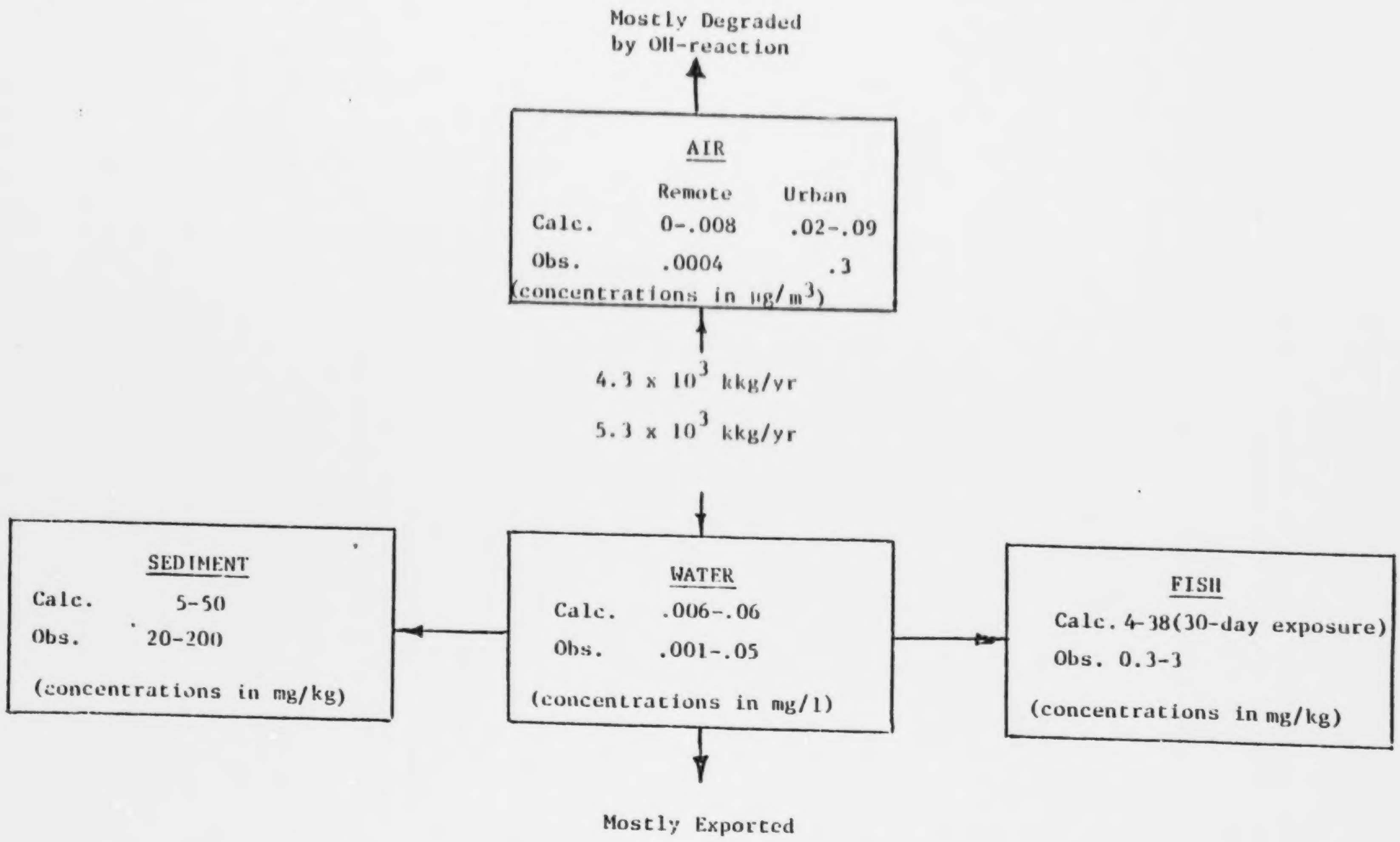

Mostly Degraded
by OH-reaction
AIR
Remote
Urban
Calc.
0-.008
.02-.09
Obs.
.0004
.3
(concentrations in μg/m^3)
4.3 x 10^3 kkg/yr
5.3 x 10^3 kkg/yr
SEDIMENT
Calc.
5-50
Obs.
20-200
(concentrations in mg/kg)
WATER
Calc.
.006-.06
Obs.
.001-.05
(concentrations in mg/l)
FISH
Calc. 4-38(30-day exposure)
Obs. 0.3-3
(concentrations in mg/kg)
Mostly Exported

FIGURE 5-7 EXAMPLE OF RESULTS OF MODELING OF ENVIRONMENTAL DISTRIBUTION--COMPARISON OF CALCULATED AND OBSERVED LEVELS OF DI(2-ETHYLHEXYL) PHTHALATE IN AIR, SEDIMENT, WATER AND FISH

Source: Perwak, J. et al. An exposure and risk assessment for phthalate esters. Final Draft Report. EPA Contracts 68-01-3857, 5949. Washington, DC: Monitoring and Data Support Division, Office of Water Regulations and Standards, U.S. Environmental Protection Agency; 1981.

TABLE 5-1. EXAMPLE OF RESULTS OF MODELING OF ENVIRONMENTAL DISTRIBUTION--COMPARISON OF RESULTS FROM MACKAY'S EQUILIBRIUM MODEL AND EXAMS FOR 1,2-DICHLOROBENZENE IN A POND SYSTEM

EXAMS Results (Pond, 24 kg/day loading 370 kg steady state accumulation)		Mackay Results (370 kg in system)	
	Maximum Concentrations		Concentrations
Water	3.0 mg/l	Water	0.0559 mg/l
Water Biota	630 mg/kg	Water Biota	18 mg/kg
Sediment Biota	610 mg/kg	Sediment Biota	12 mg/kg
Sediment	460 mg/kg	Sediment	35 mg/kg dry weight
	Accumulation	Percent of Chemical per Compartment	
% in Water	16.22	% in Water[a]	0.30
% in Sediment	83.78	% in Sediment	64.4

---

[a] Part of the initial aquatic load has been removed by volatilization.

Source: Harris, J. et al. An exposure and risk assessment for dichlorobenzenes. Final Draft Report. Contracts EPA 68-01-5949, 6017. Washington, DC: Monitoring and Data Support Division, Office of Water Regulations and Standards, U.S. Environmental Protection Agency; 1981.

TABLE 5-2. EXAMPLE OF RESULTS OF MODELING OF ENVIRONMENTAL DISTRIBUTION--EXAMS OUTPUT FOR 1,2-DICHLOROBENZENES

a. Steady-State Concentrations of 1.2-dichlorobenzene in various generalized aquatic systems resulting from continuous discharge at a rate of 1.0 kg/hour[a]

		Maximum Concentrations						
System	Loading (kg/hr)	Water Dissolved (mg/l)	Water Total (mg/l)	Maximum in Sediment Deposits (mg/kg)	Plankton (ug/g)	Benthos (ug/g)	Total Steady-State Accumulation (kg)	Total Daily Load (kg/day)
Pond	1.0	3.0	3.0	460	630	610	370	24
Oligotrophic Lake	1.0	0.15	0.15	0.73	30	3.3	410	24
River	1.0	0.00099	0.00099	0.024	0.21	0.048	1.2	24

b. The fate of 1,2-dichlorobenzene in various generalized aquatic systems[a]

	Percent Distribution		Percent Lost by Various Processes				
System	Residing in Water at Steady-State	Residing in Sediment at Steady-State	Transformed by Chemical Processes	Transformed by Biological Processes	Volatilized	Lost by Other Processes[b]	Time for System Self-Purification[c]
Pond	16.22	83.78	0.0	0.05	91.91	8.05	282.8 days
Oligotrophic Lake	98.11	1.89	0.0	0.0	94.64	5.36	83.78 days
River	75.52	24.48	0.0	0.0	1.44	98.56	18.19 days

---

[a] All data simulated by the EXAMS (U.S. EPA-SERL, Athens, Ga.) model (see text for further information).

[b] Including loss through physical transport beyond system boundaries.

[c] Estimate for removal of ca. 97% of the toxicant accumulated in system. Estimated from the results of the half-lives for the toxicant in bottom sediment and water columns, with overall cleansing time weighted according to the pollutant's initial distribution.

Source: Harris, J. et al. An exposure and risk assessment for dichlorobenzenes. Final Draft Report. Contracts EPA 68-01-5949, 6017. Washington, DC: Monitoring and Data Support Division, Office of Water Regulations and Standards, U.S. Environmental Protection Agency; 1981.

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6.0 MONITORING DATA AND ENVIRONMENTAL DISTRIBUTION

6.1 INTRODUCTION

Monitoring data, as used in the context of exposure analysis, can be defined as data on the concentration of toxic pollutants in the environment. Ideally monitoring data indicate ambient concentrations over wide geographic areas and different periods of time. They are sometimes supplemented by data measured in field studies, which can be used to indicate local conditions or special situations.

Many different kinds of monitoring data may be useful in exposure analysis. Both well-mixed equilibrium concentrations and unusually high, temporary spill or discharge concentrations are of interest. The first represents the long-term condition to which humans and other organisms are typically exposed. The second, although a short-lived condition, could potentially have acute adverse effects on exposed organisms. In addition, for certain readily transformed or transferred chemicals, only the second type of data will exist. Depending upon the environmental loading and fate characteristics of the pollutant, emphasis may be placed on finding monitoring data pertaining to either long-term or transient conditions.

Traditionally, monitoring data have been considered as measured concentrations reflecting ambient concentrations in surface water, sediment, foodstuffs, etc. However, for purposes of estimating exposure to pollutants, information regarding concentrations in more varied media are of interest.

Water--surface water (fresh and salt), ground water, raw and finished drinking water, precipitation, POTW influent and effluent, landfill leachate, industrial effluent, urban and rural runoff, etc.

Air--vapors, aerosols, and particulates in ambient air, industrial emissions, automobile emissions, workplace air environment, etc.

Soils and sediments--dust; surface and subsurface soils; bedrock; estuary, lake, river and stream sediments; etc.

Biota--soil and aquatic microorganisms, vertebrates, invertebrates, mammals, birds, organisms in a foodchain; humans, including whole body or organ tissues such as human milk, human adipose tissue, urine and blood serum.

Food--milk, meat, dairy products, grain, vegetables, fish, animal feed, etc. (both in a natural and/or prepared state).

Other--treated items such as preserved wood, painted objects, food packaging, clothing, or any other product or item that may contain the compound of interest.

Again, the particular media of interest depend upon the environmental loading and pollutant fate characteristics. For example, a highly volatile product may never be found at significant concentrations in soil and water but at high levels in air. A persistent compound with low water solubility may be detectable only in sediments and soil. Use and disposal characteristics of the pollutant will also determine which media to consider; for instance, some chemicals may be found only in the air of certain working environments. Therefore, flexibility is required in the methodology for analyzing monitoring data in order to allow emphasis on the important environmental reservoirs and sinks for various pollutants with a wide range of fate characteristics.

6.2 GOALS AND OBJECTIVES

The primary goal of the monitoring data review within an exposure analysis is to develop, analyze, and present comprehensive data on the geographic distribution of pollutant concentrations in various environmental media, indicating trends or changes over time if possible. Specific objectives include:

(1) In the initial definition and focusing of risk assessments, an analysis of monitoring data is used to characterize the behavior of a pollutant in the environment; to determine whether local, regional, or national risks are important; to identify the geographical areas of concern; and when combined with effects data, to reveal the significance of the potential risks.

(2) In some circumstances, when monitoring data are sufficiently extensive to be representative of typical environmental concentrations, they provide a description of environmental distribution.

(3) In the analysis of monitoring data, baseline levels can sometimes be established (ambient conditions) for comparison with concentrations in polluted environments. In such an analysis, for example, background concentrations near ore deposits may be found to be equal to or greater than those found in some industrial areas.

(4) Monitoring data can be used to confirm materials balance and environmental fate analyses, to provide a credible basis for extrapolating materials balance and fate considerations, and to provide input data for large-scale modeling of environmental fate.

(5) Monitoring data can suggest important routes of exposure for humans as well as other species, provide direct inputs to estimates of exposure (e.g., concentration in foods for estimating human exposure via ingestion), and to help define the risk to regional and other subpopulations.

Though not all of these objectives will be met in each particular analysis, they provide a framework to be used to the degree possible, depending on the available data.

6.3 METHODS AND APPROACHES

The approach to monitoring data analysis consists of three basic steps:

(1) identification and systematic collection of data;

(2) evaluation, analysis and presentation of data; and

(3) interpretation and use of data in exposure analyses.

At the start of a monitoring data analysis, materials balance studies should first be reviewed briefly to help identify likely media for emphasis in the systematic search for monitoring data. It will also be important to define the boundaries of the search for monitoring data--the geographic focus, depth and breadth--so that the necessary effort is devoted to this portion of the risk analysis. Also, a desired format for the presentation of data should be developed early in the work. The initial focusing step in a risk analysis will aid this process.

Collection of data should be based upon a systematic literature search. The U.S. Environmental Protection Agency, through its air and water quality programs, provides a comprehensive source of monitoring data. Particularly important for risk analyses will be the STORET system, NASQAN (National Stream Quality Accounting Network), SAROAD (Storage and Retrieval of Aerometric Data), NOMS (the National Organics Monitoring Survey), the Pesticide Monitoring Program, the Air Quality Monitoring Program, the Human Tissue Monitoring Program, etc. (see Chapter 10 for a listing). The STORET system, maintained by the Office of Water Regulations and Standards of the U.S. Environmental Protection Agency is a centralized system for storage and retrieval of water quality data. The largest file in STORET is the Water Quality File which contains data concerning 40 million observations at more than 200,000 monitoring stations in the U.S. These data are of great use in considering the distribution of a chemical in the environment. Another STORET file that often contains pertinent information is the Fish Kill File, which provides detailed and summary data on major pollution-caused fish kills dating from 1960. Thus, in addition to the traditional methods of literature search, the U.S. Environmental Protection Agency centers responsible for these monitoring systems should be contacted in order to obtain the most up-to-date data, provided the scope of the exposure assessment warrants.

In addition to the U.S. EPA, computerized data bases and publications of other federal agencies should be consulted such as the U.S. Geological Survey, Department of Interior, Department of Energy, Department of Health, Education and Welfare, Consumer Product Safety Commission, the National

Aeronautics and Space Administration, National Oceanographic and Atmospheric Administration, and the Corps of Engineers. Many of these agencies and sources have compilations of literature data which may be useful.

In evaluating monitoring data for use in exposure assessments, a series of questions should be posed:

(1) How, where, and when were the monitoring data obtained?

(2) Was the sampling process adequate to represent the environmental compartment or subcompartment being monitored?

(3) Were the analytical methods used appropriate to the monitoring problem and to the pollutant being measured?

(4) What were the sensitivity, reproducibility, and confidence of the analytical results?

(5) How were the data aggregated and reported?

The answers to these questions are not always available, and differ for every study and every pollutant. Frequently, monitoring data are not complete because results are reported for samples taken from only a few geographical locations. As a result, it is often difficult to determine whether the monitoring data are applicable only to specific geographical locations or whether they are representative of general levels in the U.S. The numerical concentration values presented in monitoring data must be used with caution because detection limits, accuracy, and precision of the measurements are frequently not reported. The analytical methods used, potential interferences, and details of the measurement approach (for example, whether the measurement represents the total metal concentration, specific ionic species, or whether a specific chemical or family of chemicals, e.g., phenols, are included). Frequently little information is given on the seasonality or other temporal variations in the measurements. Another problem associated with monitoring data is that other parameters useful in interpreting the data, such as suspended solids, pH, or the presence of other chemical species, may not be given. Perhaps the most frustrating aspect of monitoring data is the lack of additional information that helps the investigator determine whether or not the monitoring data are sufficiently representative to be used in an exposure assessment. When reporting monitoring data, it is essential to provide complete references and give any additional information that was reported in the original reference. Because of these limitations, monitoring data do not always provide a clear and accurate verification of real environmental concentrations of pollutants and may, in some cases, yield no better information than estimates obtained from fate and pathways analysis.

However, monitoring data represent the only evidence of actual exposure, since many aspects of materials balance development and fate analysis are highly speculative. Therefore, although there may be some uncertainty about values used, monitoring data should be used whenever possible in an exposure assessment.

The presentation of the available data is a difficult problem in some cases, and to an extent depends upon how the data will be used. The data may be summarized for presentation as maps, charts, graphs, tables, overlays, etc. Attention to presentation style is important, since this often effects the conclusions that are drawn from the data. Uncertainty in the data should be indicated in the presentation. Ranges, average and median values, and concentration frequency distributions should be presented, along with detection limits, wherever possible. Illustration of data trends (such as decreasing water concentrations over 10 years) provides useful information on the anticipated impact of increased production or tighter environmental regulation on pollutant concentrations.

6.4 EXAMPLES OF MONITORING DATA

6.4.1 Copper and Silver

A tremendous amount of monitoring data has been collected for copper in all media (Perwak et al. 1980). Copper levels in aquatic ecosystems (water, sediment, fish) are available from the EPA STORET data base. Figure 6-1 shows the distribution of total copper observations for the U.S. from 1970 to 1979. Obviously, this type of a figure cannot be used directly in an exposure analysis, but it does give some indication of the range of total copper concentrations that are found in the U.S.

The monitoring data can also be aggregated by major river basins, which represent large areas of the country. They can be depicted geographically as is shown in Figure 6-2 for silver (Scow et al. 1981), or displayed in tabular form. The copper data for 1970-1979 aggregated for major river basins are shown in Table 6-1 for water and Table 6-2 for sediment. By use of this technique, certain areas of the country with high copper levels can be identified. However, aggregation of data over such large areas can provide misleading results. Therefore, monitoring data from minor river basins were also examined, including data only for 1978. Table 6-3 shows that numerous minor river basins have mean concentrations greater than 50 μg/l total copper and at least 10% of the observations greater than 120 μg/l. However, only a few locations had median levels of total copper greater than 60 μg/l. In addition, some of these minor river basins were identified as having soft water (<50 mg/l $CaCo_3$), a condition that increases toxicity. These results suggested that within these minor river basins showing high mean levels, most observations were less than 60 μg/l and a few were greater than 120 μg/l.

Data from individual monitoring stations in four areas with high average copper concentrations were examined and compared with information on specific sources of copper and evidence of actual impact on aquatic biota. This analysis showed that high average copper concentrations

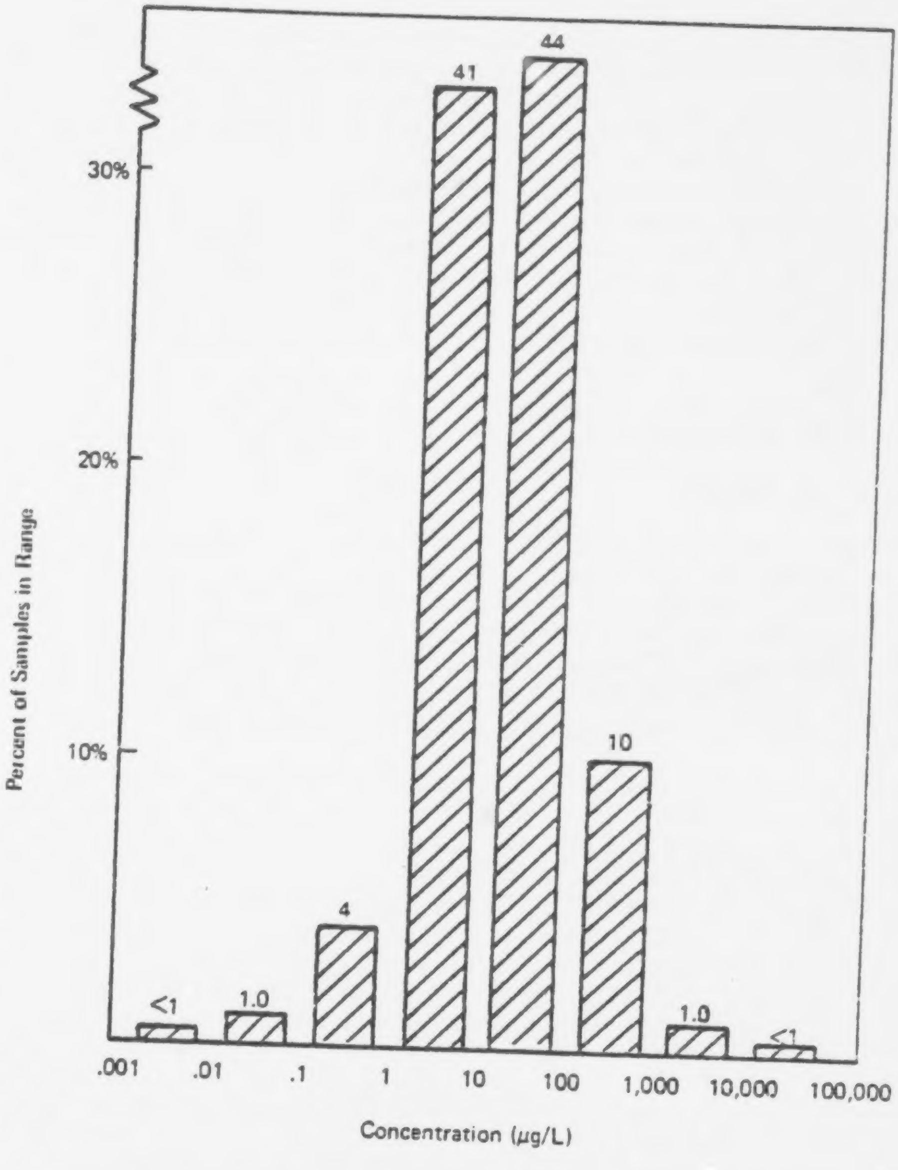
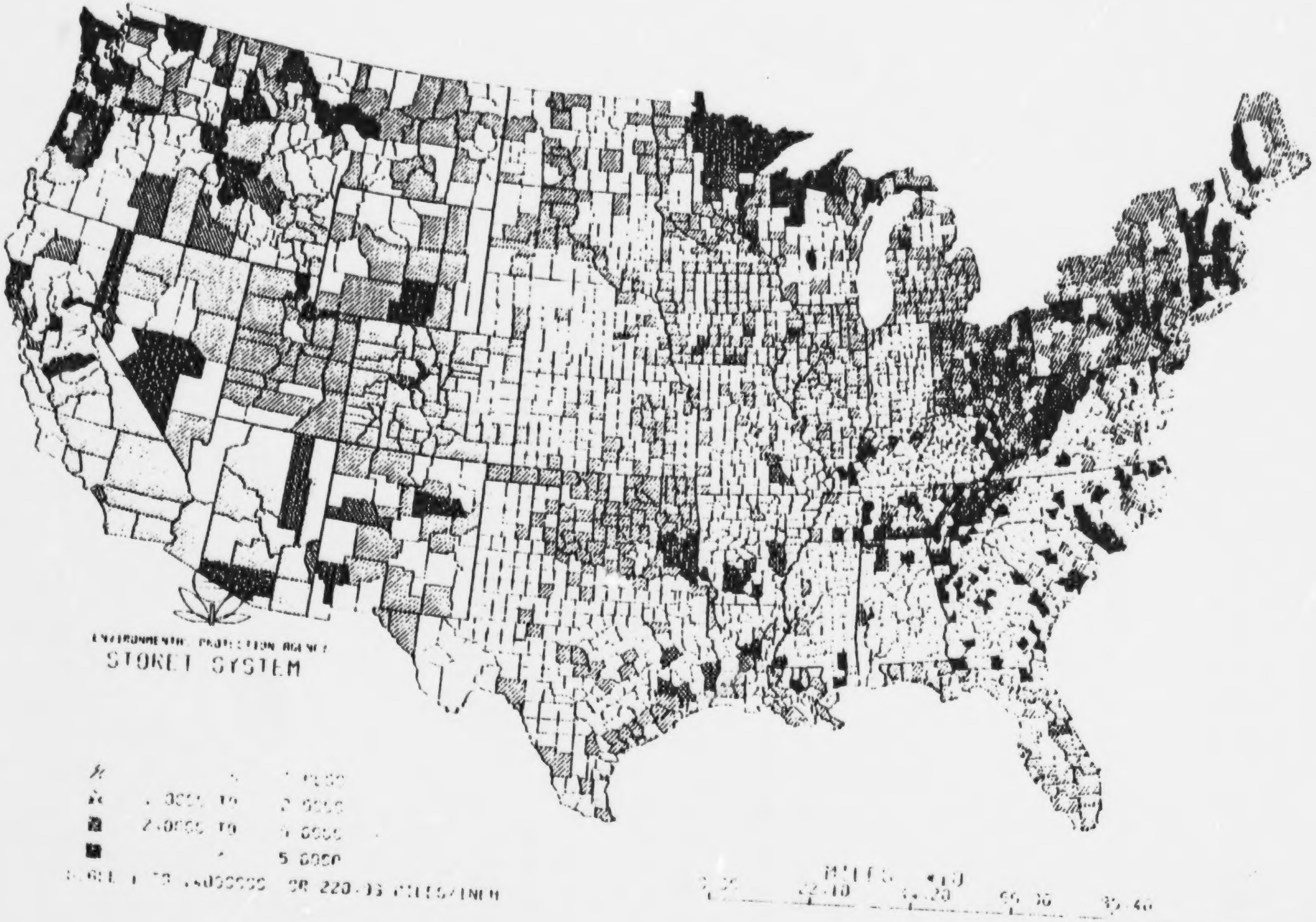


FIGURE 6-1 EXAMPLE OF SURFACE WATER MONITORING DATA DISTRIBUTION BY CONCENTRATION RANGES--COPPER 1970-1979

Source: Perwak, J. et al. An exposure and risk assessment for copper. Final Draft Report. Contract EPA 68-01-3857. Washington, DC: Office of Water Regulations and Standards, U.S. Environmental Protection Agency; 1980.


ENVIRONMENTAL PROTECTION AGENCY
STORET SYSTEM
2.0000 TO
5.0000
220.13 MILES/INCH
MILES

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best available copy.

FIGURE 6-2 EXAMPLE OF GEOGRAPHIC DISTRIBUTION OF MONITORING DATA FOR SILVER

Source: Scow, K. et al. An explosure and risk assessment for silver. Final Draft Report. Contracts EPA 68-01-3857, 5949, and EPA 68-01-6017. Washington, DC: Office of Water Regulations and Standards, U.S. Environmental Protection Agency; 1981.

TABLE 6-1. EXAMPLE OF SURFACE WATER MONITORING DATA DISTRIBUTION BY MAJOR RIVER BASINS--COPPER

Region	Percentage of Observations				
	.100-1 µg/l	1-10 µg/l	10-100 µg/l	100 µg/l- 1000 µg/l	1000-10,000 µg/l
New England	3	40	33	18	4
Mid Atlantic	1	38	49	9	1
Southeast	2	43	37	16	1
Great Lakes	1	45	48	5	<1
Ohio	1	44	49	5	1
Tennessee	<1	32	58	9	1
Upper Mississippi	<1	33	44	12	9
Souris and Red of North	<1	36	62	2	<1
Missouri	<1	44	49	6	<1
Arkansas and Red	1	45	43	11	<1
Western Gulf	3	47	29	18	<1
Hawaii	1	58	33	5	<1
Rio Grande and Pecos	9	43	34	12	2
Upper Colorado	<1	57	35	6	1
Lower Colorado	2	23	39	33	2
Great Basin	<1	48	44	8	<1
Pacific Northwest	3	55	35	6	<1
California	1	38	52	7	2
Alaska	2	48	44	6	<1
United States	4	41	44	10	1

Source: Perwak, J. *et al*. An exposure and risk assessment for copper. Final Draft Report. Contract EPA 68-01-3857. Washington, DC: Office of Water Regulations and Standards, U.S. Environmental Protection Agency; 1980.

TABLE 6-2. EXAMPLE OF SEDIMENT MONITORING DATA DISTRIBUTION BY MAJOR RIVER BASINS--COPPER

Region	Percentage of Observations			
	1-10 mg/kg	10-100 mg/kg	100-1,000 mg/kg	1,000-10,000 mg/kg
New England	33	50	15	1
Mid Atlantic	31	53	15	<1
Southeast	41	56	1	<1
Great Lakes	14	65	17	2
Ohio	24	73	4	<1
Tennessee	20	69	10	1
Upper Mississippi	23	58	4	15
Lower Mississippi	24	72	2	<1
Souris and Red of North	24	41	<1	35
Missouri	54	39	7	<1
Arkansas and Red	57	43	<1	<1
Western Gulf	37	59	2	<1
Hawaii	<1	33	67	<1
Rio Grande and Pecos	16	84	<1	<1
Upper Colorado	53	46	1	<1
Lower Colorado	40	40	20	<1
Great Basin	-	-	-	-
Pacific Northwest	14	81	5	<1
California	18	75	7	<1
Alaska	-	-	-	-
United States	30	60	8	1

Source: Perwak, J. et al. An exposure and risk assessment for copper. Final Draft Report. Contract EPA 68-01-3857. Washington, DC: Office of Water Regulations and Standards, U.S. Environmental Protection Agency; 1980.

TABLE 6-3. EXAMPLE OF SURFACE WATER MONITORING DATA FOR COPPER BY MINOR RIVER BASINS

River Basin Major/Minor	Name	Mean Cu >50 ug/L	≥50% of Cu >60 ug/L	≥10% of Cu >120 μg/L	≥50% of Hardness Measurements <50 mg
2/3	Delaware R. - Zone 1	*	*		
2/5	Delaware R. - Schuylkill	*	*		
2/6	Delaware R. - Zone 2	*			
2/7	Delaware R. - Zone 3	*	*		
2/8	Delaware R. - Zone 4	*	*	*	
3/7	Yadkin & Pee Dee Rivers	*			*
3/8	Catawba - Wateref, etc. Res.	*	*		*
3/9	Edisto - Combahef R.	*	*		*
3/13	Savannah R.	*	*		*
3/31[1]	Apalachicola R.			*	
3/32	Choctawhatchee R.			*	*
3/43	Pearl R.			*	*
4/3	French Broad R.			*	*
4/7	Duck R.	*		*	
4/8	Tennessee R.	*			
5/9	Big Sandy R.	*			
5/18	East Fork, White R.			*	
5/21	Ohio R.	*	*		
6/4	L. Erie Shore, Maumee R. to Sandusky R.	*			*
7/2	Hudson Bay, Rainy River	*			
7/13	Chicago Calumet R. - Des Plaines R.	*			
9/12	Lower Missouri R. from Niobrara R.	*			
10/11	Lower Mississippi R. - Yazoo R.			*	*
10/16	Lower Red R. — below Denison	*		*	
10/19	Atchafalaya R.	*	*	*	
10/20	Calcasieu R.	*			*
10/21	Lower Mississippi R.	*			
11/4	Gila R.	*		*	
12/1	Sabine R.	*		*	*
12/2	Neches R.	*	*	*	*
13/2	Clark Fork - Pend Oreille R.	*		*	
13/3	Spokane R.	*			*
14/4[1]	Central CA Coastal			*	
14/5[1]	Santa Clara R.	*	*		
14/9	Sacramento R.	*		*	*
15/7	Great Salt Lake	*			

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[1] Fewer than 10 measurements at this station.

Source: Perwak, J. et al. An exposure and risk assessment for copper. Final Draft Report. Contract EPA 68-01-3857. Washington, DC: Office of Water Regulations and Standards, U.S. Environmental Protection Agency; 1980 reported for some river basins were the result of a small number of very high concentrations. The analysis of the Sacramento River showed that the mean from 26 to 27 stations for 1978 was less than 30 μg/l. However, data for one station showed a mean level of 4585 μg/l for that year. Furthermore, dilution volume and the nature of the receiving water (particularly pH and hardness) had to be considered in conjunction with monitoring data in analyzing the risks of copper exposure for aquatic biota since sensitive species are known to exist in locations with high levels of copper.

6.4.2 Pentachlorophenol

Monitoring data for pentachlorophenol (PCP) are sparse and exist for scattered media and sampling sites (Scow *et al*. 1980). In 1980, the total number of observations of PCP surface water concentrations in STORET was 80. Additional surface water data were limited to scattered observations of low levels in a small number of geographic areas. The compound was reported to be present in influents to POTWs, but also appeared to be removed effectively by treatment. PCP had been detected (again at low levels) in a drinking water survey. No data were available concerning levels in air or soil.

Despite the fact that PCP did not appear to be found at high levels in aquatic media, the compound was reportedly present in some food products (Table 6-4) and also found commonly in human tissue and urine (Table 6-5), even in persons not occupationally exposed. Thus non-aquatic exposure routes had to be considered. The use of PCP as a pesticide results in numerous opportunities for human exposure, particularly via inhalation. Since no data were available on ambient atmospheric levels, fate models had to be used in the risk analysis to predict concentrations for the most likely conditions under which the general population might be exposed (e.g., in the vicinity of preservative-treated wood or open burning of such wood and downwind of cooling towers or wood treatment wastewater evaporation ponds).

6.4.3 Dichloroethanes

As is the case for many organic compounds, monitoring data for the dichloroethanes are extremely limited (Perwak *et al*. 1982). Very few data exist showing levels in surface waters. In fact, only 10 observations above the detection limit were found for 1,2-dichloroethane in the STORET data base in 1980. However, several reports of ground water contamination were found, as is shown in Table 6-6. In addition, air concentrations have been reported in heavily trafficked areas, as well as in highy industrialized areas (Table 6-7).

These limited results suggest that exposure occurs in specific areas, but that exposure to the general population is generally low. Obviously the limited sampling of ground water and air does not provide a representative sample of widespread conditions. In this case, generalizations about exposure in other areas have to be made with caution due to the limited sampling and the nature of the exposure route.

TABLE 6-4. EXAMPLES OF MONITORING DATA FOR FOOD AND FEED--PENTACHLOROPHENOL

Sample	Concentration (μg/l or μg/kg) Mean	Range	Reference*
Dairy	0.5	10	Johnson and Manske (1977)[1]
Grain and Cereal	1	10 -13	Johnson and Manske (1977)
Leaf Vegetables	T	13	Johnson and Manske (1977)
Root Vegetables	1	10	Johnson and Manske (1977)
Garden fruits	T	10	Johnson and Manske (1977)
Fruits	T	11	Johnson and Manske (1977)
Sugars	6	10 - 40	Johnson and Manske (1977)
Peanut butter	18	1.8 - 62	Heikes (1979)[2]
Bovine milk	ND		Lamparski et al. (1978)[3]

ND - Not Detected

[1] T = average below detection limit. Samples collected through U.S. in FDA's Market Basket Study.

[2] Market Basket Study - U.S. population.

[3] Michigan dairy herds, detection level = 10 μg/l.

[*] See source indicated below for references.

Source: Scow, K. et al. An exposure and risk assessment for pentachlorophenol. Final Draft Report. Contract EPA 68-01-3857. Washington, DC: Office of Water Regulations and Standards, U.S. Environmental Protection Agency; 1980.

TABLE 6-5. EXAMPLE OF MONITORING DATA FOR HUMAN TISSUE AND URINE--PENTACHLOROPHENOL

Population and Sample	Concentration (µg/kg or µg/l) Mean	Range	Reference*
Exposed workers - urine (Japan)		1100-5910	Bevenue (1967a)
Non-exposed workers - urine (Japan)		10-50	Bevenue (1967a)
General population - urine (Florida)	4.9	2.2-11.2	Cranmer (1970)
Occupational workers - urine (Florida)	119.9	22.2-270	Cranmer (1970)
General Population - adipose tissue	26.3	12-52	Shafik (1973)[1]
Occupational population - urine (Hawaii)	1802	3-35700	Bevenue (1967b)[2]
Non-occupational population - urine (Hawaii)	40	ND-1840	Bevenue (1967b)
Occupational/non-occupational population - urine	217	3-38642	Bevenue (1967b)
Combination of the above three groups (Hawaii)	587	ND-38642	Bevenue (1967b)
Occupational worker exposure - urine - by wood preserving methods (Oregon)			Arsenault (1976)[3]
Dip	2830	120-9680	
Spray	980	130-2580	
Pressure	1240	170-5570	
U.S. General Population - urine	6.3	ND-193	Kutz (1978)[4]

ND - Not Detected

[1] Detection limit = 5 µg/kg.

[2] Detection limit = 3 µg/l.

[3] Detection limit = 5 µg/l.

[4] Detection limit = 5-30 µg/l.

*See source identified below for reference.

Source: Scow, K. et al. An exposure and risk assessment for pentachlorophenol. Final Draft Report. Contract EPA 68-01-3857. Washington, DC: Office of Water Regulations and Standards. U.S. Environmental Protection Agency; 1980.

TABLE 6-6. EXAMPLE OF GROUND WATER MONITORING DATA FOR DICHLOROETHANES

Compound	No. States Tested	No. Wells Tested	% Positive Samples	Maximum (µg/l)
1,1-dichloroethane	9	785	18	11,330
1,2-dichloroethane	12	1212	7	400

Source: Perwak, J. et al. An exposure and risk assessment for dichloroethanes. Final Draft Report. Contract EPA 68-01-5949. Washington, DC: Office of Water Regulations and Standards, U.S. Environmental Protection Agency; 1982.

TABLE 6-7. EXAMPLE OF MONITORING DATA FOR DICHLOROETHANES IN AMBIENT AIR

City	1,1-Dichloroethane No. Detected/No. Sampled	Concentration Range (ng/m^3)	1,2-Dichloroethane No. Detected/No. Sampled	Concentration Range (ng/m^3)
Niagara Falls, NY	0/9	ND[a]	2/8	T[b]
Rahway/Woodbridge, Boundbrook, and Passaic, NJ	10/66	T-342	75/93	T-139,121
Baton Rouge, LA	12/43	T-500	36/43	9-10,341
Houston, TX	1/30	555	22/30	T-66,300

[a] Not detected.
[b] Trace.

Source: Perwak, J. et al. An exposure and risk assessment for dichloroethanes. Final Draft Report. Contact EPA 68-01-5949. Washington, DC: Office of Water Regulations and Standards, U.S. Environmental Protection Agency; 1982.

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7.0 HUMAN EXPOSURE AND EFFECTS

7.1 INTRODUCTION

The consideration of human exposure to toxic pollutants and the resultant effects is critical to a risk analysis or assessment. In the past, risk assessments have commonly considered only human health effects, often focusing on studies with laboratory animals and the extrapolation of animal data to humans. As indicated earlier, the integrated risk analysis approach described in this report considers human exposure and effects a vital element, but not the sole element, of a comprehensive risk analysis. In some respects, the human exposure and effects section represents the culmination of the use of materials balance and environmental fate analysis, since these efforts are often needed to estimate exposure of humans to pollutants.

The exposure of humans to pollutants and the potential effects of this exposure should be considered simultaneously. The rationale for this is straightforward--unless an individual or groups of individuals are exposed to a pollutant, they are not at risk of experiencing adverse effects, even if the pollutant is thought to be capable of inducing serious effects. Similarly, a pollutant known to produce no significant effects on humans probably presents no substantial risk to humans even though there may be widespread exposure. Thus, the risk to various populations and subpopulations depends upon the combination of exposure of those populations to a pollutant and the related effects of the pollutant.

As was the case with other parts of risk analysis, the comprehensiveness of the exposure and effects analysis is determined by the quantity and quality of available data. In general, even for pollutants that have long been recognized as toxicants, data on human effects, animal studies or epidemiological studies, are expected to be more readily available than are data on exposure. For recently identified toxicants, both effects and exposure data are likely to be unavailable, and extrapolations or estimates based upon other pollutants may be necessary. Thus it is extremely rare that both the potential for effects and exposure are thoroughly documented.

The general questions that need to be addressed in examining the available data on exposure and effects are as follows:

(1) Is there evidence of actual exposure, i.e., monitoring data?

(2) Are the data available to estimate exposures of the general population?

(3) Do the data indicate the existence of subpopulations receiving higher exposures than the general population?

(4) Are there documented human effects (tests, accidental exposures, occupational health studies) or must extrapolation from laboratory animal studies be made?

(5) Are there sufficient multi-species animal tests to permit reliable extrapolation of the results to humans?

(6) Can evidence of exposure and adverse effects on humans be validated from epidemiological studies and extrapolated to other exposure situations?

(7) Are there significant differences in human effects for different subpopulations?

In addressing the exposure of humans, one should bear in mind the initial sources of the pollutant and the fate and transport mechanisms that determine the magnitudes and routes of exposure. Only when exposures are related back to pollutant sources will it be possible to consider the alternative actions--regulatory and control--that could reduce the potential or actual exposure. Therefore, all possible exposure pathways and all of the environmental media responsible for the exposure should be carefully delineated. Both occupational and general exposure should be considered, bearing in mind exposure routes of inhalation, ingestion, and dermal contact. Specific subpopulations with higher than average exposure should be identified--these subpopulations may be delineated by geography, age, sex, occupation, food consumption patterns, activity patterns, etc. Identifying exposures in this manner requires heavy reliance on the materials balance and environmental fate portions of the risk analysis, since these elements may be the basis for estimating environmental concentrations at various locations where humans can be exposed, especially if no monitoring data are available.

To some extent, the exposure analysis should reflect the nature of effects. For example, if a pollutant is well studied and has been shown to induce effects in laboratory animals at relatively high exposure levels, worst case scenarios can be constructed for exposure in order to differentiate the low degree of risk at more realistic exposure levels. Thus, the efforts devoted to identifying and quantifying exposures of subpopulations might be reduced.

In evaluating the effects of pollutants on humans, one should consider chronic functional disorders of various organ systems, as well as the more often evaluated effects such as carcinogenicity, mutagenicity, and teratogenicity. Chronic effects need to be emphasized since environmental exposures for most chemicals (except perhaps those in the workplace or resulting from accidental releases of chemicals) occur over a long period of time, often at low exposure levels. To some extent, the human effects portion of an integrated risk analysis can be performed independently of other portions, since it depends upon the results of detailed laboratory investigations or epidemiological studies rather than on estimates of environmental loadings or pathways.

7.2 GOALS AND OBJECTIVES

7.2.1 Human Exposure Analysis

The goal of human exposure analysis is to identify and quantify the exposure of the general population and selected subpopulation groups to a pollutant or family of pollutants. Ideally the specific objectives include:

(1) Determination of the exposure of the general population to the pollutant. The general population is meant to represent the "typical" exposure, if such a population group can be defined for a given pollutant. The following parameters must be identified:

- the source of the pollutant resulting in the exposure;
- the routes of exposure--e.g., ingestion inhalation and/or dermal contact;
- the duration and frequency of exposure--e.g., continuous, 1 hour per week, 1 hour per day, etc.;
- the amount or extent of exposure--e.g., the consumption as a function of respiratory flow, amount absorbed, etc.;
- the size of the population exposed.

(2) Determination of the exposure of the work force to the pollutant in terms of:

- occupations in which exposure is encountered, the geographical locations and/or types of facilities and operations;
- the numbers of workers exposed and their characteristics--age, sex, etc.;
- the source of the pollutant, the route of exposure, the duration and frequency of exposure, and the dose or dose rate as indicated above;

(3) Identification of specific subpopulation groups that experience a higher exposure to the pollutant than the "typical" person. These subpopulations may be identified by geographic location, size, age, sex, dietary or activity patterns. The parameters of such exposure would be the same as those indicated above.

7.2.2 Human Effects Analysis

The goal of human effects analysis is to identify and characterize the health effects in humans that may occur as a result of exposure to a pollutant. More specific objectives include:

(1) Examination of the distribution, metabolism, bioaccumulation, and excretion of pollutants in humans and laboratory animals in order to identify target organs or systems. In addition, it is desirable to identify the underlying mechanisms responsible for the effects of pollutants in humans and the relationships between exposure level (dose) and response in various species.

(2) Determination of the acute and chronic health effects on humans expected and/or observed to occur from occupational or accidental exposures and the exposure pathways and levels that result in these effects.

(3) Determination of the known acute and chronic health effects of pollutants on humans on the basis of epidemiological studies and the exposure pathways and levels that result in these effects.

(4) Consideration of the acute and chronic health effects that may be expected to occur from exposure to pollutants, based upon review of laboratory animal studies, *in vitro* and *in vivo* studies with mammals, test organisms, tissues, cell cultures, or other biota. Extrapolation of the results to humans may be possible in some cases.

(5) Estimation of the "no-effect" levels of the pollutant for various exposure pathways, based on animal data or human data, when available.

The information obtained in the effects analysis should ultimately be presented in a form that can be combined with exposure analysis for the purposes of considering the risk to the general population or specific subpopulations associated with the pollutant.

7.3 APPROACHES AND METHODS

7.3.1 Exposure Analysis

7.3.1.1 General Approach

Identifying and quantifying the exposure of the general population and the subpopulation groups is a difficult task, complicated by uncertainties and lack of data, and requires numerous assumptions and new and often unproven estimation techniques. However, in order to estimate the range of risks presented by a pollutant, some "informed" estimate of exposure must be made and this requires taking a systematic and comprehensive approach to analyzing the best available data.

The exposure analysis builds upon concepts and data from the materials balance, monitoring data, and environmental fate analysis. The basic steps in exposure analysis are as follows:

(1) Identify, as comprehensively as possible, all potential sources of exposure of the human population to a chemical. In this context, "sources" can signify environmental media, human activities, or consumer products.

(2) For each source, identify the route of exposure associated with the source, e.g., inhalation, dermal contact, ingestion.

(3) For each source and route, identify key subpopulations based upon demographic/geographic characteristics that are expected to affect exposures.

(4) For each specific population group (e.g., general population; work force; specific subpopulation characterized by age, sex, type of activity, location, etc.) and for all possible routes and sources of exposure for each group, attempt to quantify the exposure as an average daily uptake or some other parameter that may be related to effects levels and the numbers of persons exposed.

Arraying data and information on an exposure matrix such as the one in Table 7-1 is a convenient way to organize this effort. Beginning at the left-hand side with the general population's exposure through the three main exposure routes, the matrix shows in the columns to the right the steps taken to identify exposure routes and to characterize, first qualitatively and then increasingly quantitatively, the exposure situation and the exposure level. When data permit, an attempt should be made to estimate the amount of the pollutant intake actually absorbed and to estimate as precisely as possible the size of each population or subpopulation. Depending upon the chemical, occupational exposures may need to be considered in the same manner. Special exposure situations and scenarios may be identified in the materials balance, environmental distribution, or fate analysis because of characteristics of sources or environmental releases, geographic considerations arising from volume of releases or intensity of sources, or unusual use situations. Often these scenarios are a further refinement of the more generalized exposure routes and need to be considered as separate exposure routes.

The subsequent discussion considers these steps in assessing exposures, first those leading to the identification of exposure routes, and then methods for estimating exposure levels for the general population and subpopulations.

TABLE 7-1. EXPOSURE MATRIX

Population	Route	Subpopulation/Associated Source	Concentration Exposure in Medium	Exposure Constant	Exposure Duration/ Frequency	Calculated Intake	Absorbed Dose	Size of Population
General	Ingestion	Drinking water typical maximum		Adult-- 2 liter per day				
		Food typical maximum		Children-- 1 liter per day				
	Inhalation	Urban-- typical maximum		child 4 m^3/day				
		Rural-- typical maximum		adult 20 m^3/day				
	Dermal Absorption	Water-- typical maximum						
Occupational	Ingestion Inhalation Dermal Absorption							

Special Situations or Scenarios:

spills
use of special products
live near disposal site or source

7.3.1.2 Sources of Exposure, Exposure Routes, and Subpopulation Groups

Sources of exposure include media, products, or activities that result in human exposure. This concept can best be explained by example. Consider a chemical that is used in household detergent. Direct exposure could result from contact with, or inhalation (perhaps even ingestion) of, the product itself. Indirect exposure could result from contact with the water solution in which the detergent is used, by contact with the residual detergent on the clothing or material washed in the detergent, by inhalation of vapor from the mixture, or by ingestion of the residual detergent from food placed on dishes washed with the detergent.

Thus, direct and indirect use of the chemical or pollutant must be considered along with the routes associated with exposure to the general population. In identifying these exposures, several general exposure sources--related to environmental media--must be considered: ambient water, drinking water, ambient air, and food. Pollutants that may exist in these media may not be attributable to specific sources, but rather to an aggregation of "sources," which yields a distribution of the chemical in the environment. The approaches and methods used in environmental pathways and monitoring are, in fact, designed to describe or develop this "ambient" media distribution. The source/exposure combinations include the background level of exposure for the general population in addition to exposure of subpopulations in specific areas or engaged in specific activities. For example, although an average general exposure resulting from ingestion of food containing a pollutant might be developed from average diet considerations, exposure of special subpopulations who eat large amounts of meat, freshwater fish, milk, etc., must be considered.

The identification of subpopulations should be approached in several different ways in order to ensure a thorough examination of exposure. In the discussion of the materials balance analysis, activities such as extraction, refining, manufacture, transportation, distribution, storage, use, and disposal were defined; each of these has the potential for releasing the chemical to the environment or perhaps exposing persons directly. As an example, disposal operations, both of products and "in-plant" materials, must be examined for the variety of exposures and routes. Exposure might result from material disposed in a chemical waste facility, perhaps indirectly through the ambient air environment of the site or surrounding public water supplies, with possible exposure routes including inhalation, contact, or ingestion. Another source may be the "municipal dump" or transfer station at which exposure of the public could result through contact with empty containers (with residual chemicals), or by inhalation of dusts or particulates.

Thus, all of the steps in the life cycle of the pollutant should be considered in order to determine the potential for human exposure. The purpose of reviewing these steps is to tie exposures to specific sources of the pollutant and to define subpopulations who sustain exposure levels greater than those of the general population. These subpopulations may be subject to occupational exposures, may live, work in, or frequent areas of pollutant sources, or obtain drinking water from supplies contaminated by pollutant sources.

Both the consideration of ambient pollutant levels to which the general population may be exposed and the review of pollutant sources are required for identifying subpopulations exposed. Identifying the potential exposure of specific subpopulation groups with unusual and/or narrowly defined characteristics is a difficult task and requires careful consideration. Furthermore, characterizing the populations and exposures quantitatively in subsequent steps of the exposure analysis is often not possible because data are lacking on the size of the population or the exposure level. Nevertheless, it is important to attempt to identify these subpopulations and to estimate the range of possible exposures, so that the range of risks (exposure combined with effects) can be estimated. Furthermore, differentiating the risk of exposure to subpopulations from those of the "average" population may identify the types of control strategies needed to reduce overall exposure and risk associated with the pollutant.

The complexity of the sources, exposure routes, and subpopulation groups and the effort devoted to identifying them will vary with each exposure/risk assessment, and will depend upon the pollutant in question and the purpose of the assessment. In some cases, it may be sufficient to consider only the "workplace" exposure, the general population exposure, or exposure of a single subpopulation group; in others, it may be necessary to identify sources, routes, and groups to the fullest extent possible. In determining what is reasonable and appropriate in each case, one should bear in mind several key points:

(1) that the risk will be a function of both exposure and the effects and, therefore, in-depth analysis of exposure may not be warranted if human health effects are not of concern;

(2) that the effort to quantify exposure with precision may be in vain if health effects are not well established or the back-up data for exposure lack precision; and

(3) that the effort should be focused on the combination of sources, routes, and population groups that have the potential for highest total exposure.

7.3.1.3 Exposure Levels From Major Exposure Routes

After exposure sources, exposure routes and population subgroups have been identified, the next step is to characterize the exposures quantitatively for each source-route-population group combination. For simplicity, this process can best be described by consideration of the major exposure routes--inhalation, ingestion, and dermal contact--as they apply to the general population, workplace population, and special subpopulation groups.

Inhalation

Exposure of individuals by inhalation can often be estimated in a straightforward way. Data are available on the respiratory rate and volume for individuals as a function of activity level (see Table 7-2). Once these parameters have been established, ambient concentrations need to be established. Usually, monitoring data do not allow the computation of a statistically meaningful mean or median that would describe average exposure to the U.S. population. If data were adequate, however, such a value could be used. Generally, it is more useful to consider the data available, their geographical and source-related representation, and choose a "typical value." Although this method requires judgment, it can provide a more meaningful value for typical exposure.

In addition to the typical exposure, or exposure to the general population, a maximum exposure should be established. If a statistical treatment is possible, the 95th percentile, or a similar value, may be chosen. Otherwise, the data must be evaluated to determine what this value might be.

If monitoring data do not exist, estimates based upon anticipated release rates and simple air models will be required. Depending upon the materials balance and fate studies, estimates of ambient concentrations may be on a national, regional or more localized basis. Similarly, OSHA, NIOSH, or other agencies may have available monitoring data or methods of estimating concentrations in the workplace.

Determination of atmospheric concentrations of a pollutant to which special subpopulation groups are exposed may be difficult; however, monitoring data may exist for selected materials and exposure situations--for example, urban and rural environments, agricultural areas in which pesticides have been applied, areas near production facilities, and other industrial sources. Usually, however, air concentrations of pollutants associated with special exposure sitautions will have to be estimated. These estimates would normally be accomplished in environmental fate and pathway analysis and would be based upon the specific process or activity, quantity of pollutant, its chemical and physical characteristics, and environmental factors such as wind, rain, temperature, etc. Persons located near smelter operations, cooling towers, waste disposal sites, or commercial cleaning facilities are examples of special groups for which exposures may need to be evaluated.

Another source of inhalation exposure that may be important in some situations is inhalation of water vapor or fog (mist, droplets), which has evolved from a water stream containing a pollutant. For these situations, estimation of the concentration of pollutant vaporized into

TABLE 7-2. RESPIRATORY VOLUMES FOR HUMANS ENGAGED IN VARIOUS ACTIVITIES

Time Reference and Activity	Air Volume (liters)				
	Adult man	Adult woman	Child (10 y)	Infant (1 y)	Newborn
Per minute:					
Resting	7.5	6.0	4.8	1.5	0.5
Light Activity	20.0	19.0	13.0	4.2	1.5
Per day:					
8 hours of working "light activity"	9,600	9,100	6,240	2,500 (10 h)	90 (1 h)
8 hours of nonoccupational activity	9,600	9,100	6,240		
8 hours of resting	3,600	2,900	2,300	1,300 (14 h)	690 (23 h)
Total 24 hr	2.3×10^4	2.1×10^4	1.5×10^4	0.38×10^4	0.08×10^4

Source: International Commission on Radiological Protection (ICRP). Report of the Task Group on Reference Man. New York, NY: Pergamon Press; adopted October 1974.

the air space above the water source, or the pollutant concentration in the mist or fog (suspended water droplets), must be estimated. Again physical/chemical properties of the pollutant, concentrations of pollutant in the original water stream, and environmental parameters will be important in these estimates. Approaches to making these estimates have been developed by the U.S. EPA (Adamson et al. 1979).

Once the air concentrations have been established to the extent possible for each situation, this information can be combined with the appropriate respiration rate to determine the estimated exposure level. The general methods will yield estimates of the quantity and rate of pollutant inhaled by various population groups, e.g., g/day, mg/hr, etc. Consideration of the source, route and characteristics of the exposure will determine whether the exposure is intermittent or continuous, short- or long-term, and whether it is a one-time exposure or an average intake over some time period.

The procedure described above considers potential exposure to a pollutant. However, much of the pollutant inhaled may not be absorbed into the blood stream. Therefore, before exposures can be compared with effects levels and the risks presented by these exposures assessed, one needs to know how much of the material that is inhaled is actually absorbed in humans as compared to laboratory animals. An evaluation of rates of absorption and metabolic pathways is conducted in conjunction with the human effects analysis (see Section 7.3). Often, though, the available data are not sufficient to indicate what portion of the potential exposure is actually available to the body. In these cases, it is necessary to assume, as the worst case, total absorption.

An example of inhalation exposure estimates is provided in Table 7-3, which gives ranges of exposure levels for trichloroethylene in different environmental scenarios (Thomas et al. 1981). The atmospheric concentrations are maximum reported values in the vicinity of the two major sources of atmospheric releases (TCE manufacturing facilities and degreasing sites) and reported ambient levels for other areas. A total daily intake has been estimated for each of these exposure situations on the basis of estimated durations of inhalation exposure and standard respiratory volumes for humans (in Table 7-2).

Ingestion of Food and Drinking Water

The most widespread exposure to pollutants for the largest number of people will probably occur through the ingestion of food and drinking water. As a result, it will be important to consider each of these ingestion routes carefully and assess exposure to the general population and specific subpopulation groups. In general, the exposure to the workplace population from food and drinking water will be similar to that of the general population so that this subpopulation does not need to be considered separately for this exposure route.

TABLE 7-3. EXAMPLE OF ESTIMATED INHALATION EXPOSURE TO TRICHLOROETHYLENE

Location[a]	Maximum Observed Concentration (μg/m³)	Weekday Duration of Exposure[b] (hrs/day)	Estimated Total Intake[c] (mg/day)	
Near Manufacturing Site				
Urban - Day (near manufacturer)	1440	8	14	14.6
- Night (Bayonne, NJ)	47	16	0.6	
Rural - Day (near manufacturer)	1440	8	14	14.04
- Night (Talledega Nat. Forest)	3	16	0.04	
Near Degreasing Sites				
Urban - Day (Aircraft Factory)	235	8	2.3	2.9
- Night (Bayonne, NJ)	47	16	0.6	
Rural - Day (Aircraft Factory)	235	8	2.3	2.34
- Night (Talledega Nat. Forest)	3	16	0.04	
Low Ambient - Rural (Talledega Nat. Forest) or Urban (East Coast)	3	24	0.06	
Remote Locations (Ambient Background)	0.03	24	0.0006	

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[a] Concentration estimates are taken from Table 4-5 in source cited below.

[b] Weekend exposures will be 24 hr/day at night time levels. Hence, these values provide an upper-bound estimate daily on exposure levels.

[c] Values are rounded. Based on respiration of 1.2 m^3/hr (awake), 0.4 m^3/hr (sleeping), about 20 m^3/day (ICRP 1975). (See citation below.)

Source: Thomas, R. et al. An exposure and risk assessment for trichloroethylene. Final Draft Report. Contract EPA 68-01-5949. Washington, DC: Monitoring and Data Support Division, Office of Water Regulations and Standards, U.S. Environmental Protection Agency; 1981.

Food

The ideal data for estimating human exposure through ingestion of food are residues in various cooked and/or processed foods included in the American diet, and food consumption patterns of the general population and subpopulation groups. After the food consumption patterns for various subpopulations have been identified, the food residue data can be used to determine quantities of pollutants ingested.

The closest approximation to this ideal is probably the Total Diet Studies conducted by FDA, Bureau of Foods (U.S. FDA 1977). In these surveys, residues of certain chemicals in specified food groups are analyzed. Composite samples are used for these food groups; residues in individual foods are not available. The Total Diet Studies consider primarily the diet of a 16-19-year old male for calculations of dietary intake. The pollutants considered by FDA are primarily metals and pesticides, and, comprehensive information for many organic chemicals is lacking. Thus, these data are useful primarily for initial estimates of the total amount of a pollutant ingested by average populations consuming standard food groups. They do not generally identify specific foods with contamination problems, or population groups with high consumption.

In the absence of data from Total Diet Studies, or perhaps in addition to it, data on specific cooked or processed foods are desirable. Information on residues in all food groups is rarely available. Thus for any given pollutant, two options are available; the first is to determine if the available information is an adequate representation of what might be expected in the whole diet; or second, to make assumptions about what might be expected in other foods based on the fate of similar chemicals. For example, residue data are often available for fish as the only food item. Since bioaccumulation may have occurred, it may be reasonable in these cases to assume that fish constitute a major dietary exposure route for humans. For example, in developing ambient water quality criteria, the EPA assumes an average daily consumption of 6.5 g of fish, utilizes bioaccumulation data to estimate the amount of pollutant contained in that amount of fish, and combines this dietary intake with drinking water intake to establish a total intake of water-related pollutant (U.S. EPA 1980). One should, however, consider whether additional major food exposure routes exist other than fish. For example, there may be some specific studies on residues of pollutants in meat and poultry, where contamination problems are expected to occur. Sources such as these should be reviewed to determine the existence of data potentially applicable to the pollutant in question.

Rarely, however, is information available on residues in cooked or processed food; residue studies in raw foods are much more common. Pollutant concentrations from raw food cannot easily be extrapolated to those in cooked foods. The U.S. EPA has been grappling with this problem in setting tolerances for pesticides in food and has not yet determined a satisfactory way to extrapolate from data concerning residues in raw foods. At present, tolerances are set on the basis of raw food.

In the absence of specific residue data for food, materials balance and fate considerations may be able to provide some insight into the probability that a pollutant will occur in food. Data are scarce on such things as pollutant concentrations in soil, uptake rate from soil, bioconcentration by plants and animals, and it is unlikely that accurate concentration levels in raw foods could be estimated. Furthermore, models would still be required to determine the changes in pollutant concentrations in foods during processing and preparation. Thus, except for some pesticides and metals, only scattered data on isolated raw or prepared food items are likely to be available, and in some cases no data will be found. Unless the food items for which data are available represent the major source of dietary exposure, even these scattered data will be of limited use in an exposure or risk assessment.

Once the data to be used for food contamination have been identified or estimated, consumption patterns must be established. The Agricultural Research Service of the USDA conducted extensive food consumption surveys in 1965 and 1978 (USDA 1972, 1980). These surveys include average consumption patterns by age groups and geographic regions. Other surveys conducted by the USDA contain some information pertaining to food consumption; data on consumption of fishery products and food fats and oils from a survey by the Economics, Statistics, and Cooperatives Service (USDA 1976) are shown in Table 7-4, as an example of the type of data that are available. While data from USDA surveys are extremely useful for estimating ingestion exposures, they do not provide information on variation in consumption by different age group or populations in various geographic regions. In addition, they may not provide consumption data for a specific food item of interest, for example, peanut butter. Thus in many cases, assumptions must be made about food consumption in order to estimate typical or maximum intake of a specific food item.

Despite the numerous limitations described above, the following process may be followed in attempting to determine the exposure to pollutants through food ingestion.

(1) Examine the USDA/FDA Market Basket/Total Diet Studies to determine if the pollutant has been measured as part of a specific or general study. Use values obtained as an indication of general exposure through food ingestion.

(2) Review any specific studies related to the pollutant in terms of residues or tolerances and, on the basis of food consumption and diet information, determine the exposure through ingestion of those specific foods. Project, if possible, the ingestion of the pollutant from similar foods and/or the total diet.

(3) Through literature research, analysis of monitoring data, environmental fate considerations, analogies to other pollutants and products, or simple models, determine the concentration (range of concentrations) of the pollutant in the food or food

TABLE 7-4. PER CAPITA CONSUMPTION OF FISHERY PRODUCTS AND FOOD FATS AND OILS IN THE U.S., 1976

Fish

Item	Per Capita consumption[a] (pounds in 1976)
Fresh and Frozen	
Fish	5.5
Shellfish	2.6
Total	8.1
Canned	
Salmon	0.4
Sardines	0.3
Tuna	2.8
Shellfish	0.4
Other	0.4
Total	4.3
Cured	0.5
TOTAL ALL FISH	12.9

Food Fats and Oils

Item	Per Capita consumption (pounds in 1976)
Table Spreads	
Butter	4.4
Margarine	12.5
Total	16.9
Cooking Fats	
Lard	2.8
Shortening	18.2
Total	21.0

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[a] Edible weight

Source: U.S. Department of Agriculture (USDA). Food consumption. prices, expenditures. Agricultural Economic Report No. 138. Supplement for 1976. Washington, DC: USDA; 1976.

group under consideration. (Often the many uncertainties involved will make this very difficult if not impossible.) If feasible, combine these estimates to obtain daily intake of the pollutant for the various subpopulation groups.

(4) Through consideration of the materials balance of the pollutant and uses of the products that contain the pollutant, develop a list of specific activities or scenarios that could result in localized occurrence of the pollutant in food: e.g., use as a pesticide on selected products, as a preservative, in a food packaging material; discharge to a freshwater stream from which people catch and eat fish; movement through the foodchain to mother's milk; processing into a one-of-a-kind food product, etc. For each scenario, attempt to identify the subpopulation group by age, sex, location, habits, etc., that may be exposed.

(5) Consider changes in concentrations or residues of pollutants in food processing and preparation. Although it is not possible to evaluate these changes thoroughly, they need to be addressed at least qualitatively in the estimation of exposure, especially in cases where levels of a pollutant in food may actually be increased during processing (e.g., the addition of lead to foods from lead solder in cans).

(6) Combine, wherever possible, data on average daily intake and exposure for the general population with data for specific subpopulations to establish ranges of human exposure.

In performing the last few steps given above, there are a number of scenarios (activities) that are more or less routine for each pollutant or product in which the pollutant may be a contaminant and each scenario may represent an exposure situation that should be analyzed as a separate exposure route:

(1) use as a pesticide or fertilizer,

(2) use as a food preservative or additive,

(3) use in food processing or preparation activity, including equipment,

(4) use in a food container or packaging material,

(5) release into soil or water from which food or food crops are grown,

(6) release in the vicinity of grazing or rangeland,

(7) use in an animal food or feed or packaging thereof,

(8) use in water system for food washing or preparation,

(9) release into water systems in which fish, shellfish or other wildlife live or feed, and

(10) use as a supplement in a poultry or livestock feed.

Through systematic consideration of each opportunity for exposure the total exposure of humans to pollutants through food ingestion may be estimated. Clearly this is an area of risk assessment that needs considerable research, development and evaluation.

Table 7-5, 7-6, and 7-7 give examples of the results of analyses of exposure from food ingestion. The data have been developed and presented in different ways. In Table 7-5, the ingestion of di(2-ethylhexyl) phthalate was calculated on the basis of data on concentrations found in various food items, and the levels of consumption of these items (Perwak et al. 1981a). Although these foods obviously do not represent a total diet, it was felt that they were a close approximation of total dietary exposure since high fat items were sampled in which phthalate esters might be expected.

Table 7-6 shows the dietary intakes of copper reported in the literature (Perwak et al. 1980a). In this case, a separate analysis was not conducted for two reasons. First, as is evident from Table 7-6 a considerable amount of work has been done in this area, and the results are in agreement. Second, the low order of copper toxicity to humans suggested that dietary intake would not be a significant source of risk. Thus, a great degree of accuracy in estimating dietary intake was not required.

Table 7-7 shows the estimated dietary intake of mercury by a select subpopulation, fish eaters (Perwak et al. 1981b). Again, intakes were calculated through use of consumption data and general residue data for the same fish species. The results show that an increased consumption can substantially increase intake over that of the population average, which in this case was about 3 μg/day attributable to seafood.

It is important to point out that a relatively large amount of data were available for analysis of the pollutants in the examples given above. Since this is often not the case, the possibility for detailed consideration is reduced. In some cases, quantitative estimation of dietary intake is not feasible, although intake can often be compared qualitatively with other exposure routes.

Drinking Water

Exposure of humans to pollutants through drinking water can vary widely, even within a very localized area, depending on the water supply. The ideal information for estimating exposure through drinking water would include a distribution of concentrations of the chemical in drinking water,

TABLE 7-5. EXAMPLE OF ESTIMATED INGESTION EXPOSURE OF DI(2-ETHYLHEXYL) PHTHALATE VIA SELECTED FOOD ITEMS

Food	Average Daily Consumption[a] (g/day)	Intake (mg/day)	
		Average	Maximum
baked beans	7.0	trace	0.01
corn meal	9.6	0.002	0.02
canned corn	7.1	trace	0.001
white bread	12.0	0.01	0.14
eggs	43.5	0.004	0.03
cereal	37	0.01	0.13
meat	210	0.13	0.63
margarine[b]	15.5	0.03	0.69
processed American cheese[b]	13.3	0.02	0.12
milk[c]	230	0.04	0.14
fish	21.4	0.004	0.15
Total		0.25	2.1

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[a] Please note that some of the categories of foods for consumption volumes do not exactly match the categories of sampled food items in all cases. For example, consumption data are used for all meat, bread rolls, and biscuits; however, only certain food items within these general categories were sampled for DEHP. No estimate of consumption was found for baked beans, so 7.0 g/day was assumed.

[b] Consumption of these foods has been corrected for fat content: margarine, 80% fat; cheese, 25% fat; and milk, 2% fat.

Source: Perwak, J., et al. An exposure and risk assessment for phthalate esters. Final Draft Report. Contract EPA 68-01-3857. Washington, DC: Monitoring and Data Support Division. Office of Water Regulations and Standards, U.S. Environmental Protection Agency; 1981.

TABLE 7-6. EXAMPLE OF INGESTION EXPOSURE ESTIMATES FOR COPPER BASED ON TOTAL DIET STUDIES

Intake (mg/day)	Type of Diet	Number of Subjects	Reference*
0.34	self-selected (24-hr)	4 female	White (1969)
0.91	self-selected	1 female	Tipton _et al_. (1966)
1.0	self-selected	11 male, 11 female	Holden _et al_. (1979)
1.04	self-selected	36 female	Tipton _et al_. (1966)
1.2	Non-institutional diets	12 female	Guthrie and Robinson (1977)
1.5	diets (no liver)	12 female	Guthrie and Robinson (1977)
1.8-2.1	balance study	11 female	Robinson _et al_. (1973)
1.9	institutional diet	12 female	Guthrie and Robinson (1977)
2.4	self-selected	12 female	Guthrie (1973)
3.8	diet composites	1 male	Zook and Lehman (1965)
7.6	diets (with liver)	11 female	Guthrie and Robinson (1977)

*See source indicated below for references.

Source: Perwak, J. _et al_. An exposure and risk assessment for copper. Final Draft Report. Contract EPA 68-01-5949. Washington, DC: Monitoring and Data Support Division, Office of Water Regulations and Standards, U.S. Environmental Protection Agency: 1980.

TABLE 7-7. EXAMPLES OF INGESTION EXPOSURE ESTIMATES OF MERCURY FOR A SPECIFIC SUBPOPULATION

Person	Species	g/Serving	Serving/ Month	Mercury Concentration (μg/kg)		Upper Limit Daily Intake (μg)[a] - 95% Confidence Limits	Maximum Intake[a]
				Avg.	Max.		
Person 1	Pike	206	15	0.01	1.7	51.37	141
	Bass	167	3	0.75	2.0		
	Perch (marine)	144	2	0.13	0.59		
	Not identified	150	1				
Person 2	Pike	253	19	0.01	1.7	79.46	222
	Bass	218	4	0.75	2.0		
	Perch (marine)	181	2	0.13	0.59		

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[a] Assumes a 0.5 μg/g mercury action limit.

Source: Perwak, J. et al. An exposure and risk assessment for mercury. Final Draft Report. Contract EPA 68-01-5949. Washington, DC: Monitoring and Data Support Division, Office of Water Regulations and Standards, U.S. Environmental Protection Agency; 1981.

comprised of data from enough locations to be representative, and the corresponding numbers of persons exposed to each concentration range. Unfortunately, this ideal situation rarely occurs.

Monitoring data for drinking water are more generally available than data on pollutant levels in air or food, but do not provide a comprehensive view of the many waterborne pollutants that may be found in water supplies throughout the U.S. The most extensive monitoring of drinking water was conducted in 1970; the survey sample in this study included 6595 water supplies in the U.S., including well water, ground water, surface water and tap water (U.S. DHEW 1970). However, the only parameters considered were those regulated by the 1962 USPHS standards. More recently, in 1974, EPA conducted the National Organics Reconnaissance Survey (NORS) (Symons et al. 1975); this study sampled 80 water supplies in the U.S. for halogenated organics. In 1976, EPA conducted the National Organics Monitoring Survey, which looked at levels of a large number of organics in 112 locations in the U.S. (U.S. EPA 1978a). These data comprise a partial basis for assessment of national exposure. Since 1976, a number of additional studies have been conducted, usually in specific locations or for specific water supplies.

The monitoring studies described above can sometimes provide data to estimate the distribution of the chemical in drinking water over the U.S. Populations can be associated with the water supplies sampled and with ground water and surface water in general, but the extrapolation of the distribution to the total U.S. population is not generally possible with the data available.

If sufficient data on the pollutant concentration in drinking water are not available on a national scale, localized data may be used in one of two ways. If data are available for a location where high concentrations would be expected on the basis of materials balance and environmental fate considerations, the subpopulation of residents in the location can be identified and their exposure estimated. In this case, no estimate of exposure to other subpopulations can be made. If the data are not from a local "hot spot," they might be used to validate the results of model(s), which would then be used to estimate maximum concentrations in drinking water in other locations. Modelling of pollutant fate in surface water is more highly developed than for groundwater. Hence this approach is more likely to be useful for estimating exposure via drinking water from surface water supplies.

In many cases and for many locations, however, monitoring data for raw or treated drinking water are unavailable or inadequate for purposes of exposure assessment. For a worst case consideration, ambient concentration data (measured or estimated from materials balance and pathways analysis) may be used directly for chemicals that would not be formed during water treatment or encountered in the water distribution system. If a more precise analysis is needed, losses or additions during water treatment must also be considered. (See chapters on Monitoring and Fate.)

The steps involved in estimating pollutant exposure of general and specific subpopulations from drinking water include:

(1) Review appropriate national surveys, STORET data, and EPA regional data to develop appropriate national average values and concentration ranges of the chemical and number of persons exposed to the chemical, if possible.

(2) Consider local data from appropriate municipal water districts, surveys, etc., to determine local concentration levels and to generalize to national average levels if practicable.

(3) From materials balance and environmental fate considerations, identify any localized areas and pathways that might result in contamination of drinking water supplies. Through modeling efforts, and in comparison with available monitoring data, determine whether these sources have led to contamination and at what levels. To the degree possible extrapolate these conditions to other locations and exposure levels.

(4) If no (or limited) data are available on drinking water, consider ambient water monitoring data for the pollutant (surface, ground, etc.) and investigate to what extent treatment would remove the contaminant from the water in the water supply/treatment process.

(5) From materials balance considerations, examine other unconventional routes of entry of a pollutant into drinking water; for example, from chemicals used in treatment, pipes/valves used in distribution systems, etc. From monitoring data or simple models, evaluate the concentrations that may result in drinking water.

Once the concentrations of a pollutant in drinking water have been determined for various exposure subpopulations, they must be combined with an appropriate exposure constant in order to estimate the pollutant intake. Although consumptions of 2 liters per day for adults and 1 liter per day for children are commonly assumed in exposure calculations, considerable variation exists in consumption. In cases in which ingestion via drinking water is a major exposure route, it may be appropriate to consider a range of consumption values in estimating exposures. In addition, the rate of absorption of the pollutant in the gastro-intestinal tract must be considered for pollutants in drinking water in the same manner as for pollutants in food.

Tables 7-8 and 7-9 illustrate some results of analyses of drinking water exposure. Table 7-8 shows the drinking water exposures for 1,2-dichloroethane,with associated populations (Perwak et al. 1982a). In this case, as is common for many organic chemicals, the reported values of the monitoring data are near the detection limit of the analytical

TABLE 7-8. EXAMPLE OF ESTIMATED EXPOSURES TO 1,2-DICHLOROETHANE VIA DRINKING WATER INCLUDING POPULATION SIZE

Population	Estimated Population Size	Assumption	Calculated Exposure (μg/day)
General Population			
Surface Water	5 million	2 μg/ℓ, 2ℓ/day	4
Ground Water	5 million	0.3 μg/ℓ, 2ℓ/day	0.6
Isolated Sub-Populations			
Surface Water	--	maximum level of 4.8 μg/ℓ, 2ℓ/day	9.6
Ground Water	--	maximum level of 400 μg/ℓ, 2ℓ/day	800

Source: Perwak *et al*. An exposure and risk assessment for dichloroethanes. Final Draft Report. Contract EPA 68-01-5949. Washington, DC: Office of Water Regulations and Standards, U.S. Environmental Protection Agency; 1982.

TABLE 7-9. EXAMPLE OF MAXIMUM AND TYPICAL ESTIMATED EXPOSURES TO TRIHALOMETHANES VIA DRINKING WATER

Trihalomethane	Concentration (mg/l)		Daily exposure (mg/day)	
	Median	Maximum	Assuming Maximum Adult Intake[a] and Maximum Concentration in Water	Assuming Reference Male Intake[b] and Median Concentration in Water
Chloroform	0.059	0.540	1.2	0.1
Bromoform	0.004	0.280	0.6	0.007
Dibromochloromethane	0.004	0.290	0.6	0.007
Bromodichloromethane	0.014	0.180	0.4	0.02

[a] 2.18 liter per day

[b] 1.65 liter per day

Source: Perwak, _et al_. An exposure and risk assessment for trihalomethanes. Final Draft Report. Contract EPA 68-01-5949. Washington, DC: Office of Water Regulations and Standards, U.S. Environmental Protection Agency; 1980.

procedures; hence there is considerable uncertainty attached to the values shown and the calculated exposures. In such a case, it may be desirable to be conservative, that is, to overestimate, rather than underestimate typical exposure levels. In this example the population sizes were estimated by extrapolating the percentage of water supplies in which the compound was detected in the sample to the percentage of the total U.S. population exposed. This extrapolation does not incorporate many complicating factors, and the distribution in size of water supplies is assumed to be the same in the sample as in the U.S. Though this assumption may be valid for surface water, it is probably invalid for groundwater supplies in which sampling has been very limited.

Table 7-9 shows human exposures to trihalomethanes via drinking water, as estimated by use of maximum and median observed concentrations and consumption levels (Perwak _et al_. 1980b). This table indicates (as does Table 7-8) that a wide range of exposures can occur. In general it is not possible to determine the population distribution of exposure levels. At best, usually a median, mean, or "typical" and a maximum exposure can be estimated.

Dermal Absorption

Dermal absorption of a pollutant from ambient or treated water and/or directly from the use of the chemical or product contaminated by the chemical should be examined in an exposure assessment. The process of estimating the "average daily intake" of a pollutant by the dermal route is slightly different than for other exposure routes; the concentration of pollutant in the water or solutions, the nature of the chemical contacted, the time of contact, and the area, location and integrity of the skin exposed can all affect the uptake.

The first step is to examine the types of human activities in which direct contact exposure to the pollutant can occur. In addition to workplace exposures or contact with pollutants during manufacture, the exposure potential of use situations must be examined carefully, e.g., exposure resulting from: mixing or application of pesticide formulations; pollutant containment in paint, glue, stain, or similar materials; use of cosmetics, gasoline or cleaning solvents; polymers, films or fibers in apparel or other products, etc. Laboratory data on the rate of absorption through the skin may be available for a few chemicals. In the absence of such data, estimates might be made through use of octanol/water (or other) partition coefficients, although these procedures are unvalidated. Thus, in many cases, the exposure analysis will be limited to establishing the nature of the exposed population, its size, other characteristics affecting the exposure (duration and frequency of exposure, extent and area of the body exposed) and perhaps an extrapolation of rate based upon the rate of absorption of similar chemicals. Data seem to be available concerning chemicals used in pesticides and cosmetics; because of the variety of the chemicals used and the apparent variation in rates of absorption, these data may not be very useful in general estimates of average daily intake.

The second category of exposures that should be examined is the exposure of the general population and specific subpopulations who are in contact with ambient or treated water which may contain the pollutant as a contaminant. In this case, three steps are required:

(1) defining the numbers of persons exposed and the characteristics of the exposure;

(2) estimating the concentrations of pollutants in water to which persons are exposed; and

(3) estimating the rate of transfer from the water to the person.

A considerable body of literature exists on the number of persons exposed to various activities which involve water--swimming, boating, bathing, fishing, dishwashing, etc. Data on seventeen exposure activities in personal, recreational and household categories have been identified and summarized by U.S. EPA (1979) including estimates of the populations exposed, extent, frequency or duration of exposure. Estimates of the concentrations of pollutant in the water used in these activities can come from monitoring data or from estimates generated in the materials balance and environmental fate and pathways analyses.

Estimating the rate of absorption through the skin is more difficult. An analysis of this process (U.S. EPA 1979) indicates that the diffusion rate of the pollutant through the stratum corneum layer of the skin may be the controlling factor; this is dependent upon the permeability coefficient of the pollutant and the partition coefficient of the pollutant between the human skin and the water. Some data exist upon which to base estimates; laboratory investigations of the diffusion rate of pollutants through skin are in progress. Through combination of analysis of activities involving water, concentrations of pollutants in water, and rate of absorption through the skin, order of magnitude estimates of the actual exposure by dermal contact--in terms of an average daily intake for various activities or subpopulations--can be made.

Table 7-10 gives some examples of the estimated dermal exposure to pollutants based upon absorption through skin. The estimates for pentachlorophenol (PCP) were based on a permeability constant for phenol (Scow et al. 1980). For the halomethanes, a permeability constant for chloroform was used (Perwak et al. 1980b). In most cases, dermal exposure levels are small compared with those of other routes. However, they can be large, as indicated by the home-use of PCP as a preservative.

Other Exposure Routes

Some other specific exposure routes should be considered for selected pollutants. A major category is the use of medical products. For example, food supplements for humans can greatly increase exposure (i.e., zinc, copper, other trace nutrients). Intravenous solutions and other products--plasma, blood, dextrose or saline solutions--can be a means of entry of

TABLE 7-10. EXAMPLES OF ESTIMATED EXPOSURES TO POLLUTANTS BY ABSORPTION THROUGH THE SKIN

POLLUTANT EXPOSURE	ESTIMATED EXPOSURE (mg/day)
Pentachlorophenol:	
Persons bathing and dishwashing with contaminated water	0.003 - 0.03
Home use of PCP as preservative	170
Handling of treated wood	0.5
Trihalomethanes:	
Children swimming 1 hr/day in freshwater pool containing ∿160 μg/ℓ chloroform	0.2 (chloroform)
Children swimming 1 hr/day in saltwater pool containing ∿60 μg/ℓ bromoform	0.7 (bromoform)

Sources: Scow, K. et al. An exposure and risk assessment for pentachlorophenol. Final Draft Report. Contract EPA 68-01-3857. Washington, DC: Office of Water Regulations and Standards, U.S. Environmental Protection Agency; 1980.

Perwak, et al. An exposure and risk assessment for trichloromethanes. Final Draft Report. Contract EPA 68-01-3857. Washington, DC: Office of Water Regulations and Standards, U.S. Environmental Protection Agency; 1980.

a pollutant to humans both from contamination of the fluid or from the packaging material or tubing. Similarly, dental materials and surgical implants can be a source of exposure. The contributions of these sources to total exposure levels are highly variable, but can be very significant for some pollutants and subpopulations.

7.3.1.4 Summarizing Exposure

As a result of exposure analysis, exposure to a pollutant by various routes can be summarized for the general population and for specific subpopulation groups. In this way, the activities that are most responsible for human exposure can be identified, ranges of exposure levels can be developed and used to help estimate the risk associated with exposure, and pathways of exposure can be examined in order to determine the potential effects of changes in control regulations.

The results of an exposure analysis for lead (Perwak, et al. 1982b) are shown in Figures 7-1 through 7-3 and Tables 7-11 and 7-12. As shown in Figure 7-1, the exposure routes for humans are numerous and complex. The ingestion of paint chips is commonly thought to be the most prevalent lead exposure problem in the U.S. today, and this is borne out by the high exposure levels shown in Figure 7-3. and Table 7-11. Intake of lead in food is the primary pathway for adults not employed in lead-related industries and among children without pica (Figure 7-2). Inhalation exposures, shown in Table 7-11, are heavily influenced by proximity to industrial sources.

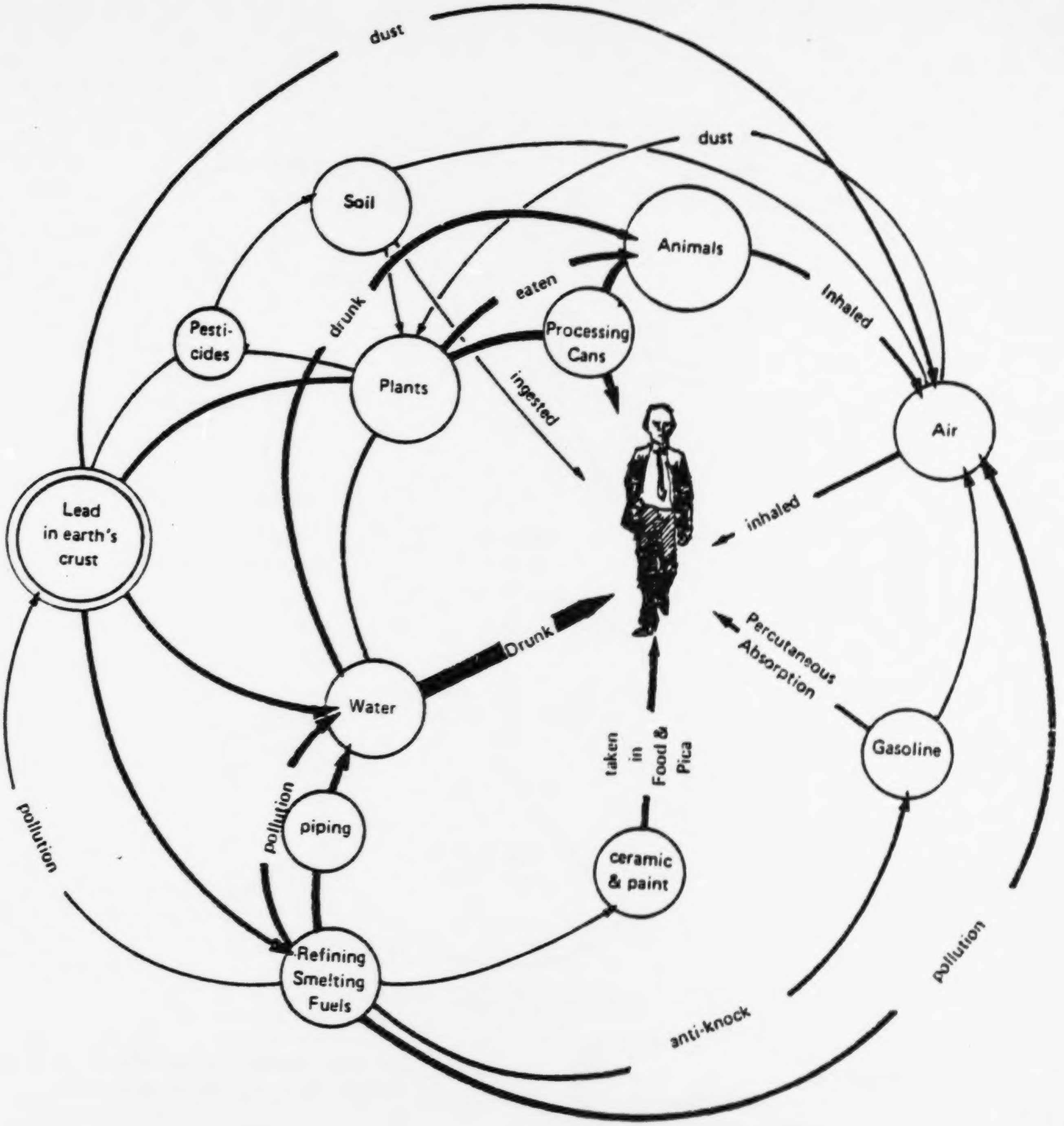
Data were available to permit estimation of the rates of absorption of lead, and exposure levels have been converted into absorbed doses in Figures 7-2 and 7-11. The relative contributions of exposure routes as absorbed doses to the exposure scenarios for adults and children with pica are displayed in these figures.

Exposure may also be measured by other parameters, such as levels in blood or tissue. In some cases, this information can be combined with actual effects information from epidemiological studies to achieve an estimate of risk. This was the case for lead, and this information (shown in Table 7-12) in combination with the exposure estimates can give a good basis for the identification of sources of risk.

7.3.2 Effects Analysis

7.3.2.1 General Approach

In developing an approach to address the effects of toxic substances in the environment on humans, a number of issues deserve attention. First, one must determine what effects should be considered in the analysis.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Pica
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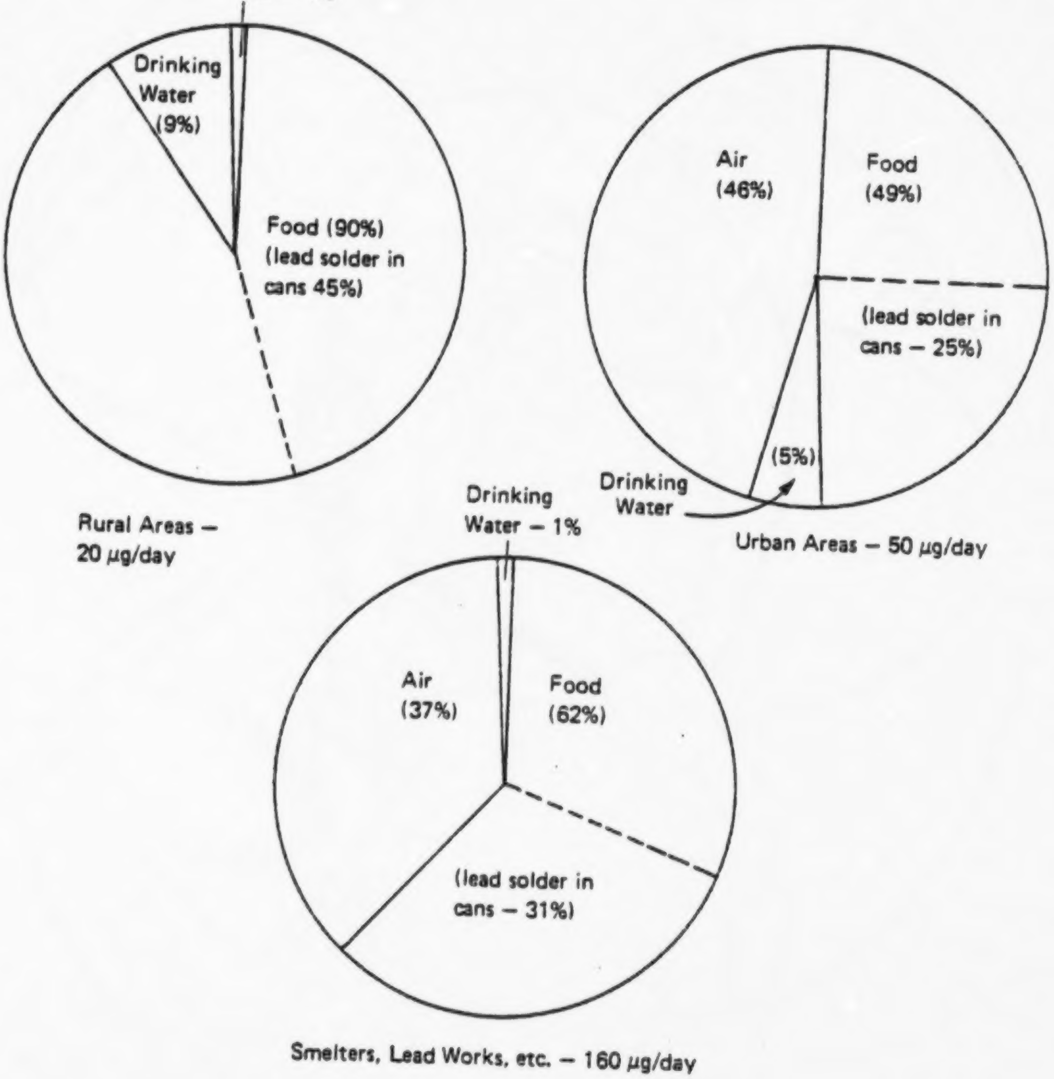
pollution
pollution
piping
ceramic
& paint
Refining
Smelting
Fuels
pollution
anti-knock

FIGURE 7-1 EXAMPLE OF GRAPHIC SUMMARY OF ROUTES OF HUMAN EXPOSURE TO LEAD

Source: Perwak, J. et al. An exposure and risk assessment for lead. Final Draft Report. Contract EPA 68-01-3857. Washington, DC: Monitoring and Data Support Division. Office of Water Regulations, U.S. Environmental Protection Agency; 1982.



Note: Concentrations < 10 μg/ℓ in drinking water were assumed for these estimates, and no consumption of wine or moonshine containing lead. In addition, these situations did not include exposure from smoking.

FIGURE 7-2 EXAMPLE OF GRAPHIC SUMMARY OF ESTIMATED EXPOSURES TO LEAD FOR THE GENERAL ADULT POPULATION

Source: Perwak, J. et al. An exposure and risk assessment for lead. Final Draft Report. Contract EPA 68-01-3857. Washington, DC: Monitoring and Data Support Division, Office of Water Regulations, U.S. Environmental Protection Agency; 1982.

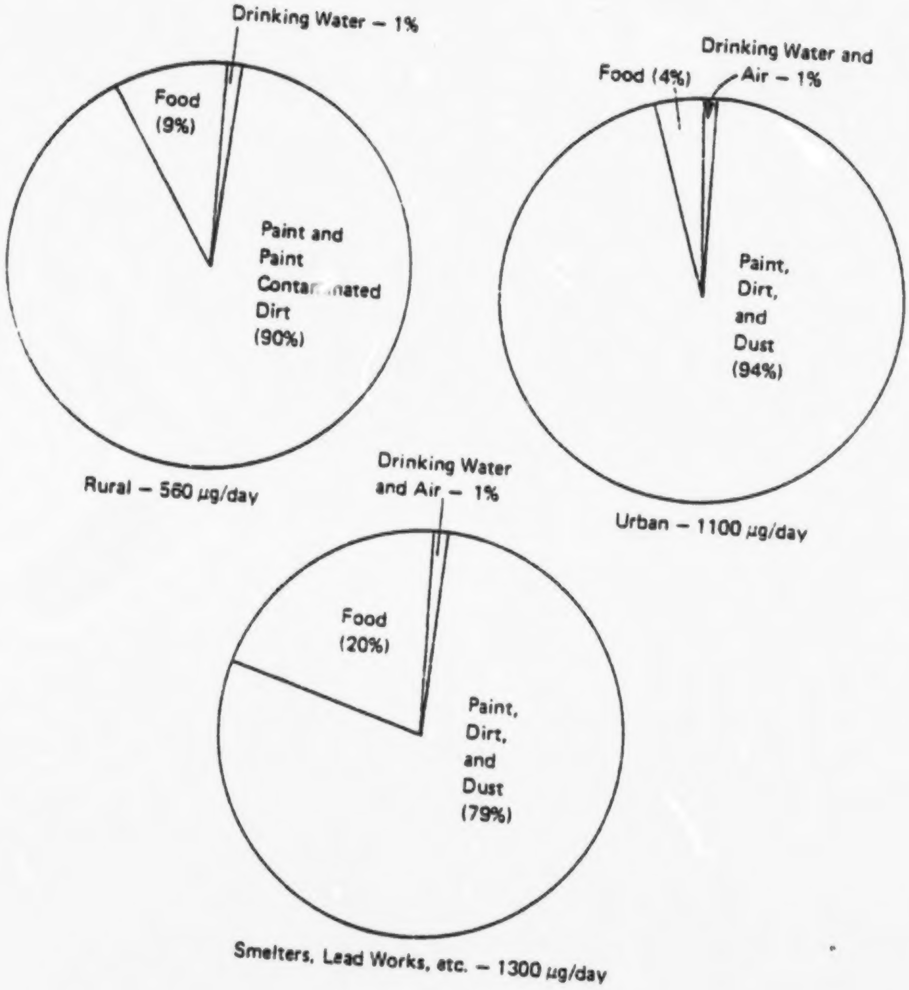


FIGURE 7-3 EXAMPLE OF GRAPHIC SUMMARY OF ESTIMATED EXPOSURES TO LEAD FOR A SPECIFIC SUBPOPULATION (CHILDREN WITH PICA)

Source: Perwak, J. et al. An exposure and risk assessment for lead. Final Draft Report. Contract EPA 68-01-3857. Washington, DC: Monitoring and Data Support Division, Office of Water Regulations and Standards, U.S. Environmental Protection Agency; 1982.

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TABLE 7-11. EXAMPLE OF EXPOSURE ESTIMATES OF LEAD FOR ADULTS AND CHILDREN INCLUDING ESTIMATED ABSORBED DOSE

Population	Location	Route	Source	Assumption	Intake (µg/day)	Absorbed Dose[a] (µg/day)
Adults						
	Rural	Food	Total Diet		100-200	10-20
			Moonshine	1 mg/l, 1 l/day	1000	100
			Wine	0.2 mg/l, 1 l/day 0.2 mg/k, 5 l/day	200 1000	20 100
		Drinking Water	Most Supplies	<10 µg/l, 2 l/day	<20	<2
			Contaminated	>50 µg/l, 2 l/day	>100	>10
			Highly Contaminated	>1000 µg/l, 2 l/day	>2000	>200
		Inhalation	Suburban	See Table 5-1[b]	1.5-15	0.5-5
			Remote	See Table 5-1[b]	0.4	0.1
			Cigarettes	-	-	1-5
	Urban	Food	Total Diet		100-200	10-20
			Moonshine	1 mg/l, 1 l/day	1000	100
			Wine	0.2 mg/l, 1 l/day 0.2 mg/l 5 l/day	200 1000	20 100
		Drinking Water	Most Supplies	<10 µg/l, 2 l/day	<20	<2
			Contaminated	>50 µg/l, 2 l/day	>100	>10
			Highly Contaminated	>1000 µg/l, 2 l/day	>2000	>200
		Inhalation	Urban Air	See Table 5-1[b]	15-62	5-21
			Cigarettes	-	-	1-5
	Smelting Areas	Food	Total Diet	-	100-2640	10-264
			Moonshine	1 mg/l, 1 l/day	1000	100
			Wine	0.2 mg/l, 1 l/day 0.2 mg/l, 5 l/day	200 1000	20 100

TABLE 7-11. EXAMPLE OF EXPOSURE ESTIMATES OF LEAD FOR ADULTS AND CHILDREN INCLUDING ESTIMATED ABSORBED DOSE (Continued)

Population	Location	Route	Source	Assumptions	Intake (μg/day)	Absorbed Dose[a] (μg/day)
		Drinking Water	Most Supplies	<10 μg/l, 2 l/day	<20	<2
			Contaminated	>50 μg/l, 2 l/day	>100	>10
			Highly Contaminated	>1000 μg/l, 2 l/day	>2000	>200
		Inhalation	Ambient Air	10 μg/m^3, 20 m^3/day	200	60
			Cigarettes	-	-	1-5
Children						
	Rural	Food	Total Diet	-	100	50
		Drinking Water	Most Supplies	<10 μg/l, 1 l/day	<10	<5
			Contaminated	<50 μg/l, 1 l/day	<50	<25
			Highly Contaminated	>1000 μg/l, 1 l/day	>1000	>500
		Inhalation	Ambient Air	See Table 5-1[b]	0.36-3.4	0.1-1
		Pica	Lead Paint	1% lead, 1 mg chip	1000	500
			Paint or Otherwise Contaminated Dirt	1000 μg/g lead in dirt, 10 mg/mouthing, 10 mouthings/day	100	50
	Urban	Food	Total Diet	-	100	50
		Drinking Water	Most Supplies	<10 μg/l, 1 l/day	<10	<5
			Contaminated	<50 μg/l, 1 l/day	<50	<25
			Highly Contaminated	>1000 μg/l, 1 l/day	>1000	>500
		Pica	Lead Paint	1% lead, 1 mg chip	1000	500
			Dirt	1000 μg/g lead in dirt, 10 mg/mouthing, 10 mouthings/day	100	50
			Dust	10,000 μg/g lead in dust 10 mg dust/mouthing, 10 mouthings/day	1000	500

TABLE 7-11. EXAMPLE OF EXPOSURE ESTIMATES OF LEAD FOR ADULTS AND CHILDREN INCLUDING ESTIMATED ABSORBED DOSE (Continued)

Population	Location	Route	Source	Assumption	Intake (µg/day)	Absorbed Dose[a] (µg/day)
	Smelting Areas	Food	Total Diet	Assumed to be half of adult	500	250
		Drinking Water	Most Supplies	<10 µg/l, 1 l/day	<10	<5
			Contaminated	<50 µg/l, 1 l/day	<50	<25
			Highly Contaminated	>1000 µg/l, 1 l/day	>1000	>500
		Inhalation	Ambient Air	10 µg/m³, 4 m³/day	40	12
		Pica	Lead Paint	1% lead, 1 mg chip	1000	500
			Dirt	1000 µg/g lead in dirt, 10 mg/mouthing, 10 mouthings/day	100	50
			Dust	10,000 µg/g lead in dust 10 mg dust/mouthing, 10 mouthings/day	1000	500

[a] 10% absorption of ingested lead is assumed for adults and 50% for children. Deposition of inhaled lead is assumed to be 30% and 100% if deposited lead is assumed to be absorbed.

[b] Table 5-1 in source cited below.

Source: Perwak, J. *et al.* An exposure and risk assessment for lead. Final Draft Report. Contract EPA 68-01-5949. Washington, DC: Monitoring and Data Support Division, Office of Water Regulations and Standards, U.S. Environmental Protection Agency, 1982.

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TABLE 7-12. EXAMPLE OF LEAD LEVELS IN BLOOD IN SUPPORT OF EXPOSURE ESTIMATES

LOCATION	BLOOD LEVEL (µg/100 ml)	REFERENCE*
Adults		
Rural/Urban	9-24 Most ∿ 16	Bell *et al*. (1979)
Urban	18--mean (adjusted for age and smoking) Less than 5% >30	Tepper and Levin (1972)
Rural	16--mean (adjusted for age and smoking) Less than 0.5% >30	
Within 3.7 meters of Highway	23--mean	Daines *et al*. (1972)
Living Near a Smelter	16% >40	Landrigan *et al*. (1975)
Children		
Urban (primarily)	40,000 children detected annually >30	
	∿ 20 yearly geometric mean	Billick *et al*. (1980)
Within 30 meters of Highway	50% >40	Caprio *et al*. (1974)
Near Smelter--Kellogg, ID--1974 (immediate vicinity)	99% >40 60% >60	Walter *et al*. (1980)
1975	Somewhat reduced[a]	Anonymous (1979)
1979	Almost all >60[a], and most >40	
El Paso, TX	70% >40 14% >60	Landrigan *et al*. (1975)

---

[a] Reduction as a result of reduced atmospheric emissions as well as increased sanitary procedures for the workers who were apparently exposing their children to lead through their clothing.

*See source indicated below for references.

Source: Perwak, *et al*. An exposure and risk assessment for lead. Final draft report. Contract EPA 68-01-3857. Washington, DC: Monitoring and Data Support Division, Office of Water Regulations, U.S. Environmental Protection Agency; 1982.

Second, the spectrum and quality of health effects data available for use in assessing risk to humans should be examined. For chemicals that have long been recognized as toxicants, data may be available from epidemiologic studies or from reports of effects on humans, as well as data for laboratory animals; for other chemicals, especially newly developed ones, only laboratory animal or in vitro data may be available, if any at all. As a result, one must be prepared to adapt the scope of the analysis in accordance with the available data.

Third, one must consider the format of the effects analysis. Ideally, quantitative relationships based upon human data would be developed between the exposure (expressed in terms of specific dose, average daily intake, etc.) and the response of humans (death, morbidity, changed reproductitive capacity, etc.). Generally, sufficient information will not be available and, by necessity, data for laboratory animals will be extrapolated to man. Frequently there will be insufficient animal data to develop dose/response relationships and risk will have to be assessed in terms of no observed effect levels and appropriate safety factors. In cases in which no specific data associated with the chemical are available, the only option remaining will be qualitative statements based on structure/activity relationships or similarity with other chemicals.

Assessment of potential health hazards associated with exposure to a particular chemical typically begins with a literature search. There are many computerized and manual data bases for health effects and toxicologic data (e.g., CANCERLINE, TOXLINE, MEDLINE, ENVIROLINE, etc.) that can be used to obtain citations concerning human safety aspects of the chemical in question (see Chapter 10 for a listing). The number and scope of citations in these data bases are expanded regularly. By careful selection of key words and structuring the search to include the possible effects of the pollutant, a substantial amount of data can be obtained.

When the literature has been obtained, all appropriate and reliable human and animal data should be evaluated. As an aid to the organization and analysis of the information, a matrix of the types of data that should be analyzed is presented in Table 7-13. As indicated earlier, direct human data are more desirable, but generally not available. Ideally, if one could fill in the human data columns of the matrix, then data for the other columns would not necessarily have to be considered. Not all types of health effects need to be thoroughly studied, in that the data needs will be unique for each chemical. However, each area should be examined briefly to determine if it is relevant to the chemical in question, and if its inclusion in the risk assessment would be useful.

Once all available information has been thoroughly evaluated, judgments should be made regarding the relevance of the mode of exposure utilized in animal studies to that associated with human exposure. Interaction of agents that may result in synergistic or antagonistic effects should also be indicated, if known. On the basis of the kinds

TABLE 7-13. MATRIX FOR INITIALLY ORGANIZING ANALYSIS OF HUMAN HEALTH EFFECTS INFORMATION

Health Effects Information	Data on Humans		Mammalian Data	In Vitro Data	Inference/Extrapolation from Other Related Chemicals
	Epidemiological	Accident			
Metabolism, absorption, accumulation, distribution, excretion (pharmacokinetics and mechanism of action)					
Acute					
Subchronic					
Chronic					
Carcinogenicity					
Mutagenicity					
Teratogenicity					
Fetotoxicity					
Functional Disorders and Effects					
CNS					
Reproductive					
Hepatic					
Renal					
Cardiac					
Gastrointestinal					
Respiratory					
Digestive					
Circulatory, etc.					

of responses induced by the chemical, an assessment can be made of the acute and long-term adverse effects that might result from exposure to the chemical, in a form usable for risk analysis. The output of the effects analysis should include:

(1) The type and nature of the effects of the pollutant expected in humans;

(2) The levels of exposure (dose, intake, etc.) that produce these effects in humans and/or experimental animals;

(3) The quantitative relationships, if any, that have been documented between effect and exposure in humans or experimental animals;

(4) The variation in effects and exposure/effects relationships for different human subpopulations (age, sex, diet, etc.).

(5) The levels of exposure at which no effects are observed; and

(6) The level of uncertainty in the available data.

That every chemical will induce negative health effects if administered in sufficient quantity is axiomatic in toxicology. The challenge is always to establish what exposure levels are probably non-threatening and what exposure levels are associated with certain risk. Thus, toxicology cannot avoid being a quantitative discipline.

Human biology, however, is very difficult to quantitate. Thus, quantitative predictions must be developed for a highly heterogeneous, poorly reproducible system. As a result, reported values are generally thought of as representing some point (hopefully, the midpoint) of a fairly broad range of effects rather than an exact number to be taken at face value. Any quantitative conclusions regarding health risks must be reached with care and with recognition of reliability and/or limitations of the data upon which they are based.

In the sections below, the types of data that are desired for human effects analysis are briefly presented, along with an approach or hierarchy for examining and analyzing these data. Examples of typical data summaries from actual risk/exposure assessments are presented in the discussion. [In Chapter 9.0, possible methods for extrapolating animal data to humans (quantitative risk assessment) will be discussed.]

7.3.2.2 Details of Approaches and Examples

Absorption, Metabolism, Bioaccumulation and Excretion

In studying the effects of a pollutant on humans, it is important to know the routes by which the pollutant can enter the body; the degree of absorption, if any; the extent of metabolism; whether the pollutant is accumulated and in what tissues; and how it is excreted. These factors are imporatnt for several reasons:

(1) They form the linkage between exposure of humans to concentrations of pollutant in the environment and the possible effects.

(2) They establish the relative significance of the various routes.

(3) They may indicate target organ systems.

(4) They can aid in the interpretation of data on concentrations of the pollutant in human and animal tissues (monitoring data).

(5) They may provide a rational basis for estimating the effects of the pollutant on humans based upon animal or in vitro studies.

(6) They may suggest other related chemicals (metabolites or precursors of the pollutant) that need to be examined.

Recommending a generalized approach to seeking and evaluating these types of data is difficult; nevertheless one would generally start with human data if available and then proceed to experimental animal data. For example, for established chemicals, pesticides, and most metals, one can anticipate that epidemiologic studies, as well as animal data, will be available. Important considerations needing investigation include: degree of absorption; rate of clearance from blood or plasma; principal routes of elimination; sites and amounts of residues or accumulations in body tissues; the half-life in the body for the pollutant and/or its metabolites.

For example, if biliary excretion was found to be a major route of elimination, species differences in the rate of biliary excretion of the compound into the bile might result in species variation in the biologic half-life of the compound and its toxicity. Another example of the usefulness of these data is the use of tissue distribution patterns in defining populations at risk. Toxicants are often concentrated in a specific tissue; some may be concentrated at their site of toxic action, such as carbon monoxide, which has a high affinity for hemoglobin. Other chemicals are sequestered harmlessly at storage sites, but may be released at toxic levels on remobilization of the store, e.g., chlordane stored in body fat, can be remobilized under weight loss conditions; lead stored in bone can be remobilized with increased calcium demand, such as during pregnancy and/or lactation.

Another reason for reviewing metabolic and pharmacokinetic data is that some substances in the environment are also essential elements or nutrients in many species, e.g., copper and zinc. Understanding the pathways and uses of the element in the body can help to establish whether the amounts obtained from environmental sources are excessive for normal body function and whether large or small increments can lead to toxicity. In the case of copper, for example, one finds that absorption of ingested copper is very incomplete (Venugopal and Luckey 1978). Furthermore, ionic copper has a strong emetic action. As a result, ingestion of copper and its salts in small quantities does not usually present a high risk. Inhalation of copper dusts, fumes or copper-containing products may present a more serious risk (Perwak, et al. 1980a).

Other examples could easily be drawn from the literature, but these should suffice to indicate the importance of metabolism, accumulation, pharmacokinetics, and mechanism of action data in effects analysis.

Acute Effects

Although cases of acute human effects resultings from exposure to environmental pollutants are not very prevalent, it is important to examine acute human toxicity data for several reasons:

(1) acute accidental or occupational exposure to high concentrations of pollutants may be the only human data available;

(2) acute effects may identify specific organ systems at risk to chronic exposure; and

(3) the comparison of acute human effects with animal data combined with metabolism and other data, can support the use of chronic animal data for extrapolation to humans.

The majority of acute human toxicity data that is most often available in the medical literature, "poison centers," and/or NEISS, results from suicidal or accidental exposure, often in children. Standard tests on industrial safety and hygiene may also contain acute toxicity values for inhalation, ingestion, and dermal absorption. Although large bodies of data from humans are often not available, the types of acute toxicity, symptoms, and effects, and in some cases, minimal lethal values for man are generally available. The minimum lethal dose, however, only indicates that a single death due to the chemical has been recorded at that dose which may be the results of a high dose accident or suicide attempt. In fact, the minimum lethal dose may be equivalent to an LD_5 (the dose found to be lethal to 5% of the exposed population); or it may be many times higher than an LD_{90} (the dose found to be lethal to 90% of the exposed population). Thus, quantitative conclusions on human risk must be reached with care, according to the limitations of the data.

Data may also be available concerning the acute toxic effects of a chemical in laboratory animals, particularly rodents. Acute toxicity studies provide information on the relative effects of different exposure routes (inhalation, ingestion, skin contact), provide a measure of comparison among many substances whose mechanism and sites of action may be markedly different, and are roughly indicative of the effects of chronic exposure to small amounts of the chemical. Acute toxicity tests are also frequently conducted to determine local effects of chemicals when applied directly to the skin or eye. Thus, acute toxicity studies place the overall acute toxicity of different pollutants in perspective. In the development of new chemicals, for example, these acute tests are often used as an initial screen to aid in the determination of whether or not to continue to develop a chemical. Such tests are also required by regulatory agencies for pesticides, drugs, food additives, etc.

There are not generally accepted standard data to search for, or special means of data presentation. A clear understanding of the implications of the data is the important concern. For example, very low exposure levels of cyanide are very acutely toxic, but are rapidly cleared from the body (Williams 1959), while lead may present no acute toxic response at low levels, but its accumulation in bone can result in grave consequences to man (Mahaffey 1977).

Subchronic Effects

Subchronic testing involves the administration of the test chemical on multiple occasions. Experiments are generally conducted for 90 days with rats or mice, for 6 months to 1 year with dogs. Subchronic studies are typically conducted at higher exposure concentrations than chronic studies. Pathologic changes are thus more clearcut because they occur more quickly with the higher doses and are not obscured by other chronic changes such as aging. For example, focal myocarditis is a common spontaneous type of lesion found in high frequency in aging populations of rats (Simms 1967). A marked increase in the incidence of this lesion after 90 days' exposure would be noteworthy, but might be attributed to aging or a small population remaining at termination of a chronic study.

Carcinogenicity

Cancer is characterized by an uncontrolled growth of abnormal cells: a carcinogen is defined as any toxic substance which has been demonstrated to cause tumors in mammalian species by induction of a tumor type not usually observed, or by induction of an increased incidence of a tumor type normally seen, or by its appearance at a time earlier than would be otherwise expected (National Cancer Institute 1976).

As is the case with other effects, examination of carcinogenic risk begins by consideration of human epidemiologic data, if available. Figure 7-4 presents in flow chart form a procedure for evaluating data on carcinogenicity. Ideally, one would follow the yes pathways to develop the most reliable estimates of the carcinogenic effects of the pollutant. Thus the chart is organized so that the items in the bottom row appear from left to right in order of descending desirability and reliability. If data are limited to in vitro data, data on related compounds, or structure-activity relationships (SAR), the risk of carcinogenicity can probably not be assessed reliably.

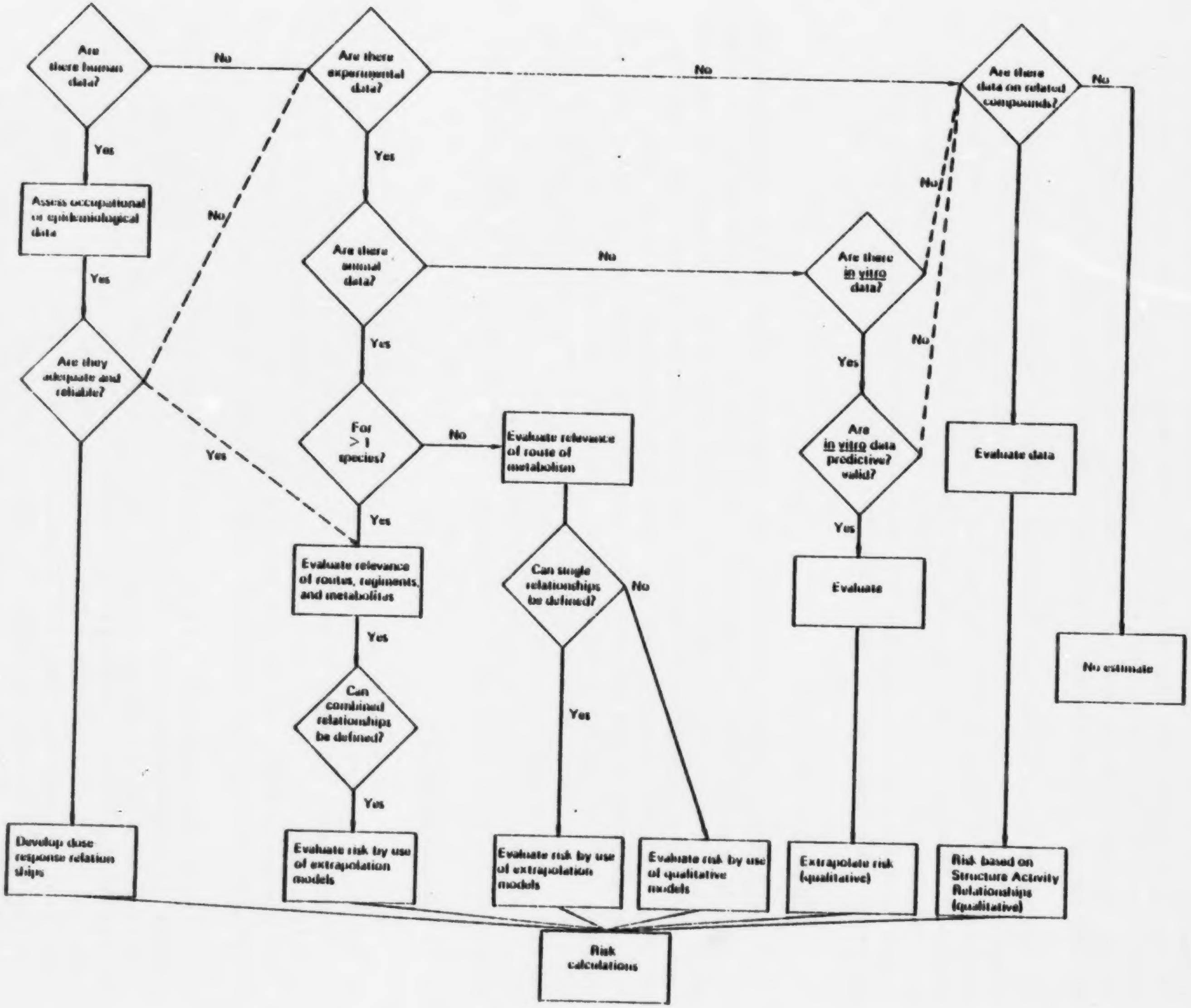
Are there human data?
No
Yes
Assess occupational or epidemiological data
Yes
Are they adequate and reliable?
No
Yes
Develop dose response relation ships
Are there experimental data?
No
Yes
Are there animal data?
No
Yes
For > 1 species?
No
Yes
Evaluate relevance of routes, regiments, and metabolites
Yes
Can combined relationships be defined?
Yes
Evaluate risk by use of extrapolation models
Evaluate relevance of route of metabolism
Can single relationships be defined?
No
Yes
Evaluate risk by use of extrapolation models
Evaluate risk by use of qualitative models
Are there in vitro data?
No
Yes
Are in vitro data predictive? valid?
No
Yes
Evaluate
Extrapolate risk (qualitative)
Are there data on related compounds?
No
Evaluate data
Risk based on Structure Activity Relationships (qualitative)
No estimate
Risk calculations

FIGURE 7-4 FLOW CHART FOR CARCINOGEN RISK EVALUATION

The route shown on the left-hand side of Figure 7-4, based entirely upon human data, is the ideal path in evaluating carcinogenic risks, but will in reality very seldom be used because adequate data are lacking. Epidemiologic data, even if available, most often do not represent causal relationships, only correlations or associations, and must thus be augmented by other types of data. Reports of occupational exposure give a somewhat more direct indication of causality, but the dose-response relationships may be difficult to define. Thus, in most cases, human data alone will not provide a suitable risk estimate, although coupled with experimental animal data, they may permit a more rigorous analysis.

If experimental animal data are available, there are four possible routes to assessing risks depending on, first, the number of species tested and, second, whether or not dose-response relationships are known. In following any of these paths, careful attention must be paid to the quality of the data, the incidence of spontaneous tumors in the control population, consistency if more than one study is available, and statistical validity. If the exposure route and experimental regimen employed (e.g., intra-muscular injection) do not agree with the most likely mode(s) of human exposure, the data must be interpreted cautiously. Consideration should be given to data on metabolism of the compound by the animal species tested, as compared with metabolism in humans if this information is known.

If only _in vitro_ data are available, only qualitative estimates may be possible because of uncertainties regarding the association between _in vitro_ results and human or animal effects; the availability of associated pharmacokinetic data, however, may allow an approach to a rough quantitative estimate. Even less reliability will be possible if no experimental data are available and only SARs can be established between the compound and related compounds for which data are available.

In following the path indicated in Figure 7-4, information from the National Cancer Institute's carcinogenicity programs should be examined, as well as data from the medical literature. Discussions with qualified toxicologists/oncologists should supplement a critical analysis of the literature for chemicals for which the data are equivocal or conflicting. For example, animal studies weakly support an association between exposure to benzene and carcinogenicity (Snyder _et al_. 1980), but the evidence that benzene is a leukomogen for man is convincing (Askoy 1977; Infante _et al_. 1977a,b; Ott _et al_. 1978). Benzene may in fact play a co-leukomogenic role, which would explain the failure to induce leukemia in several benzene-exposed animal species.

Mutagenicity

A mutation can be defined as any heritable change in the genetic material (DNA) of a cell or organism. Among the sequelae of a mutation are cell death, altered structure and/or function, and no overt immediate effect, should the mutation be unexpressed by virtue of its recessive nature. The types of changes that occur in the genetic apparatus of a cell can range from modifications in the individual base pairs, resulting in point mutations in a single gene, through major chromosomal structural changes that may involve entire sets of genes, to disruption of entire sets of chromosomes. Some examples of these kinds of occurrences in humans are sickle cell anemia (an example of point mutation) and Trisomy 21 (Down's syndrome, an example of a major chromosomal disorder).

Some relatively rapid and technically accessible bioassays for mutagenicity are being used as predictive tools to identify not only agents with possible mutagenic activity, but also those that may induce cancer or cause a teratogenic response. A large amount of experimental evidence indicates that many agents that are carcinogens also can damage DNA, and the correlation between activity of chemicals in the mutation screens and activity as carcinogens is high [e.g., the Ames test has been found to be 80 to 90% accurate in detecting carcinogens as mutagens (McCann _et_ _al_. 1975)]. This and similar tests are widely used as an initial testing mode to identify potential genotoxic agents, although correlations between potency and response are often not good. Thus, testing for mutagenicity has wider implications than merely determining the potential for mutagenic risk following exposure to chemicals. Figure 7-5 is a flow chart describing the general approach to evaluating the risks associated with mutagenicity.

With respect to assessing mutational changes that may result in genetic damage in humans, a critical component that often can be used for carcinogenesis and teratogenesis risk assessment is not available. This component is the identification of exposure to a chemical agent with a known human health-related genetic response as can be done with vinyl chloride and angiosarcoma; thalidomide and limb anomalies.

Thus, the highest ranking data that could be used for risk analysis for mutagenesis in humans will not likely be available. Planned and already ongoing epidemiology studies may produce some useful correlations and an analysis of the available data on spontaneous abortion may yield additional direct data. A number of indirect data sources are available from observations made on human tissues and body fluids. While these are only indicative they do provide the most powerful source of information presently available with respect to human exposure to chemical mutagens.

In the absence of human data, two tiers of experimental data can be used in the risk analysis process. Specific locus tests or heritable translocation tests provide data that can be used with most confidence, because they measure specific heritable changes. With the large resources

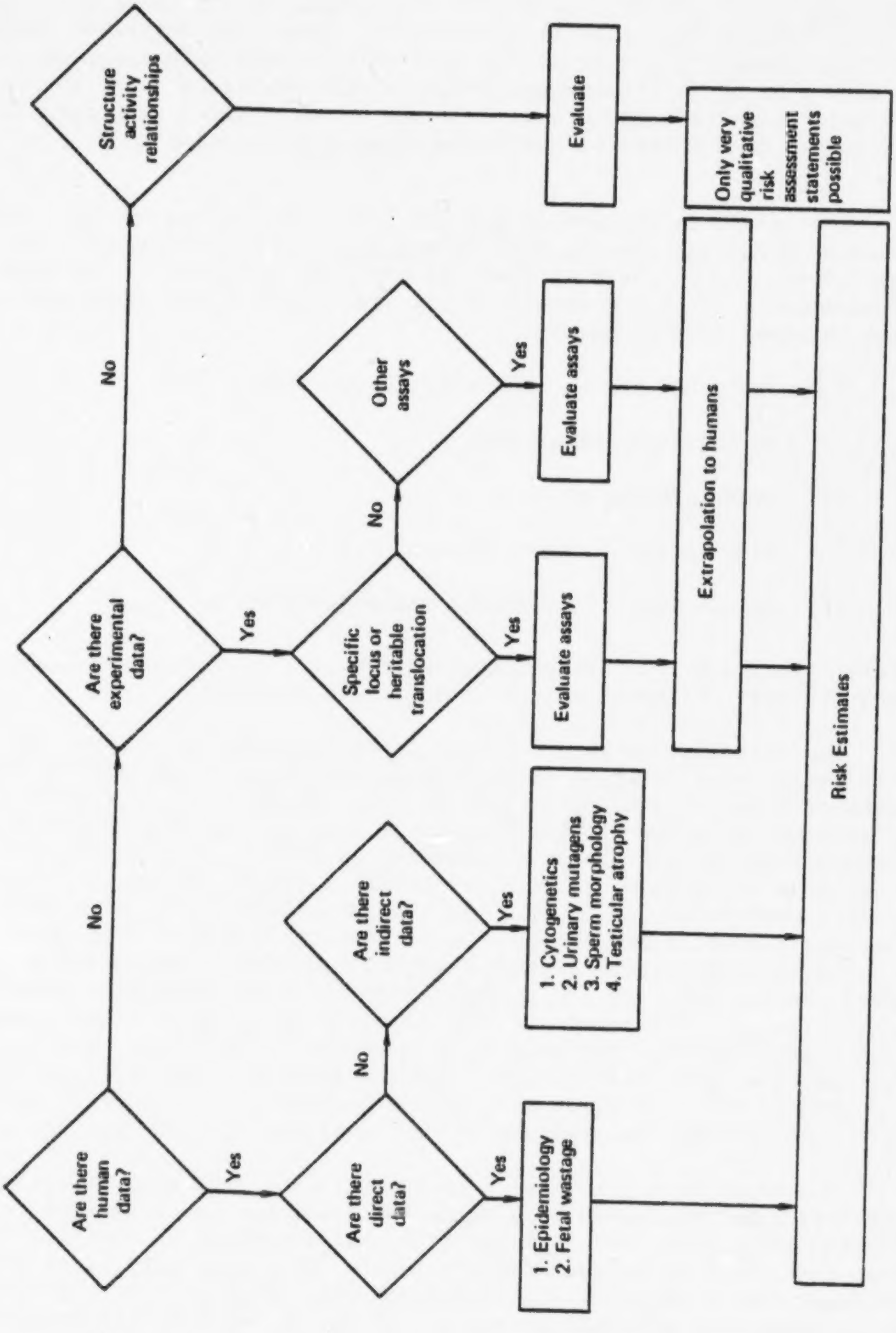
Are there human data?
Yes
No
Are there direct data?
Yes
No
1. Epidemiology
2. Fetal wastage
Are there indirect data?
Yes
1. Cytogenetics
2. Urinary mutagens
3. Sperm morphology
4. Testicular atrophy
Are there experimental data?
Yes
No
Specific locus or heritable translocation
Yes
No
Evaluate assays
Other assays
Yes
Evaluate assays
Extrapolation to humans
Structure activity relationships
Evaluate
Only very qualitative risk assessment statements possible
Risk Estimates

FIGURE 7–5 FLOW CHART FOR MUTAGENICITY RISK EVALUATION

and time required for the specific locus assay, there is not much likelihood that this test will be used for materials except those that may have a large medical and/or social importance. Thus, the heritable translocation assay appears to be the only readily available experimental tool at this time for a direct measurement of transmissable genetic damage. Its major disadvantage is that it measures only male-originated changes, and it too is a relatively large and expensive bioassay.

The remaining battery of genetic tests, though useful, are only indicative and the results must be evaluated with considerable care for appropriate use in the risk analysis process. A number of criteria should be examined in order to establish the usefulness of the experimental data obtained from bioassays:

(1) heritable versus non-heritable changes,

(2) phylogenetic hierarchy,

(3) genetic endpoint,

(4) sensitivity of assay system, and

(5) validation of assay data and assay system.

These criteria are interdependent and complex, so that a simple treatment of these variables is not likely to be possible.

For example, a marked increase in chromosomal aberrations was noted (see Table 7-14) in mouse spermatogonia following gavage administration of doses of aqueous phenol solution far below levels associated with other effects and at environmental exposure levels that a large fraction of the human population may encounter (Bulsiewicz 1977). In addition, an apparent trend toward increased aberrations within a single treatment group in each of five successive generations was evident. In that (1) most mammalian species, including man, handle phenol biologically in a similar manner, (2) the treatment route of this study is the same to which man will likely be exposed, and (3) in vivo cytogenetic analyses in mammals are considered more relevant than similar tests in vitro or genetic tests with lower organisms for predicting a mutagenic hazard for man, Bulsiewicz's results were cause for concern. Unknown factors, however, such as tissue and species made any discussion of the genetic implications of the reported chromosomal aberrations for man more speculative than factual.

The means by which genetic assay data should be used in a risk assessment has been considered by a number of prominent investigators in the field (Freese 1973, Crow 1973, Bridges 1974, and Report of a Committee of the European Environmental Mutagen Society 1978). They generally agree that risk analyses and subsequent action based on experimental tests other than the specific locus and heritable translocation assays would not be easily supportable.

7-14. EXAMPLE OF PRESENTATION OF MUTAGENICITY DATA--INCIDENCE OF CHROMOSOMAL ABERRATIONS IN SPERMATOGONIA OF PHENOL-TREATED MICE

Generation	Dosage Level (ug/kg/day)	% Chromosome Breaks	% Chromatid Breaks	% Aneuploidy	% Polyploidy	% Associations
P	0	0	0.8	0	0.8	0
	6.4	1.7	3.3	1.7	3.3	0.8
	64	5.8	5	5	10.8	2.5
	640	9.2	7.5	10	13.3	1.7
F_1	0	0	0	2.5	2.5	0
	6.4	3.3	10	11.7	1.7	3.3
	64	10.8	15	15	15.8	5.8
	640	12.5	14.2	17.5	19.2	7.5
F_2	0	0	1.7	0	0.8	0
	6.4	9.2	8.3	9.2	5	5.0
	64	15	15.8	17.5	14.2	7.5
	640	19.2	17.5	19.2	22.5	5.8
F_3	0	0	0	0.8	1.7	0.1
	6.4	5.0	5.8	13.3	8.3	3.3
	64	10.8	14.2	22.5	15.8	9.2
	640	10*	10*	36*	32*	8.0*
F_4	0	0	0.8	0.8	0.8	0
	6.4	6.7	8.3	10	6.7	10
	64	15.8	20	20.8	23.3	15.8
	640	20	25	27.5	30.8	17.5
F_5	0	0	0	1.7	0	0.2
	6.4	10	6.7	13.3	11.7	6.7
	64	17.5	23	25.8	21.7	19.2
	640	51.3*	37.5*	37.5*	56.3*	25*

*Excludes 3 mice killed in moribund condition. Preparations made from the testes of these mice showed absence of primary and secondary spermatocytes, spermatids, and spermatozoa.

Source: Scow, et al. An exposure and risk assessment for phenol. Final Draft Report. Contract EPA-68-01-5949. Washington, DC: Monitoring and Data Support Division, Office of Water Regulations and Standards, U.S. Environmental Protection Agency; 1981.

Moreover, these investigators believe that a positive finding in the heritable translocation assay should be given considerable weight in a risk analysis.

No special data presentation methods need to be considered in mutagenicity analysis; careful reporting of the interpretations of others and correlation of one series of tests with another are, however, important.

Teratogenicity

Teratology can be broadly defined as the study of malformations of the newborn that occur as a result of an adverse effect(s) on the developing conceptus. In the past, the term malformation implied gross anatomic malformations; but in recent times, the term malformation has been broadened to include more subtle, functional abnormalities and even postnatal behavioral and intellectual development.

A teratogen, the agent exerting an adverse effect on the developing conceptus, exerts its effect in the time interval between conception and the termination of morphogenetic development in the post-partem animal. The picture is complicated somewhat in that certain morphogenic events are terminated at widely varying times in different species. For instance, re-opening of the eyelids, opening of the external acoustic meatus, formation of the vaginal lumen, and descent of the testes occur prenatally in man, whereas these events take place postnatally in the mouse, rat, and rabbit, the species most often used in experimental studies. In addition, other factors such as metabolic differences, excretion rates, placental variations, age of the dam, and nutritional status may all influence the potential teratogenicity of a chemical in a particular species. Moreover, the dose, route, and time of gestation at which a conceptus is exposed are critical in defining whether a particular chemical is teratogenic in a particular species.

The assay procedures presently available to test for the teratologic potential of chemicals are empirical, largely because the detailed biological mechanisms of teratogenesis are not well understood. Clearly, understanding the mechanisms of teratogenesis would be the most fruitful approach to predicting the risk of exposure to new chemicals or even well established ones. Unfortunately, the state of the art of understanding the mechanisms of action of most known teratogens is quite primitive. There is evidence to support about 8-10 mechanisms of action: mutation, chromosomal aberrations, mitotic interference, altered nucleic acid integrity or function, lack of precursors and substrates for bio-synthesis, altered energy sources, enzyme inhibition and osmolar imbalance and altered membrane characteristics (Wilson 1977). All of the above mechanisms are not mutually exclusive, i.e., both genetic and environmental factors determine tertatogenic risk. In addition, many of these mechansisms are non-specific effects seen only at high doses (e.g., enzyme inhibition, altered energy sources) and extrapolation of these findings to man is of questionable value.

This lack of information on the mechanisms of teratogenesis is highlighted by the findings that show chemicals to which humans are widely exposed such as aspirin, vitamin A and hydrocortisone, to be teratogenic in certain experimental systems. Although there are no data to eliminate these chemicals from consideration as human teratogens, there is also no evidence that their consumption by pregnant females or by males prior to fertilization at doses normally employed has resulted in malformation in their progeny. In contrast, methyl mercury and methotrexate, which have been implicated as human teratogens, induce a teratogenic response in a wide range of species, including the smaller rodents usually employed in most experimental studies, i.e., mouse, rat, Syrian hamster.

One means of approaching a better understanding of the relationships between teratogenic effects of chemicals in humans and in experimental animals is to examine those instances for which a chemical has been identified as a human teratogen and has been tested later in experimental animals. The most well known case of this type is the one concerning thalidomide, which is especially instructive, since it illustrates some of the problems in using experimental animal data in a prospective manner. Had thalidomide been tested for teratogenicity according to the usual protocols in rats or mice, there would have been little or no indication of any problem. In rabbits and subhuman primates, however, thalidomide was demonstrated to be a potent teratogen.

One of the primary difficulties in extrapolating experimental data from laboratory animals to man is the high probability of differences in metabolic fate of chemicals, especially their disposition in gonadal or placental tissues. Moreover, because of the complex behavioral and dietary practices of humans, in contrast to the controlled regimens of experimental animal test populations, there may be wide individual variation among humans with respect to the ultimate metabolic fate of chemicals taken into the body. Another source of variation in humans is the intrinsic genetic individuality of each person in comparison with the rather uniform genetic background of test animals, even those of the "random bred" category. Since the susceptibility to teratogenic stimuli appears to have a genetic component in humans, the presence of genetic diversity is a further complicating issue in the use of experimental teratology data for estimation of such a risk in humans (Leck 1977).

Thus, although the methods of detection of potential teratogenic agents have merit, at present there appears to be no clear correlation between teratogenesis data for humans and that for experimental animals. Accordingly, man has no alternative but to take a conservative approach toward exposure to chemicals during pregnancy.

With the above precautions, the risks associated with teratogenesis can be examined as shown in the general flow chart of Figure 7-6. Following in depth examination of human data, if any, including studies on related chemicals, *in vivo* and *in vitro*, laboratory

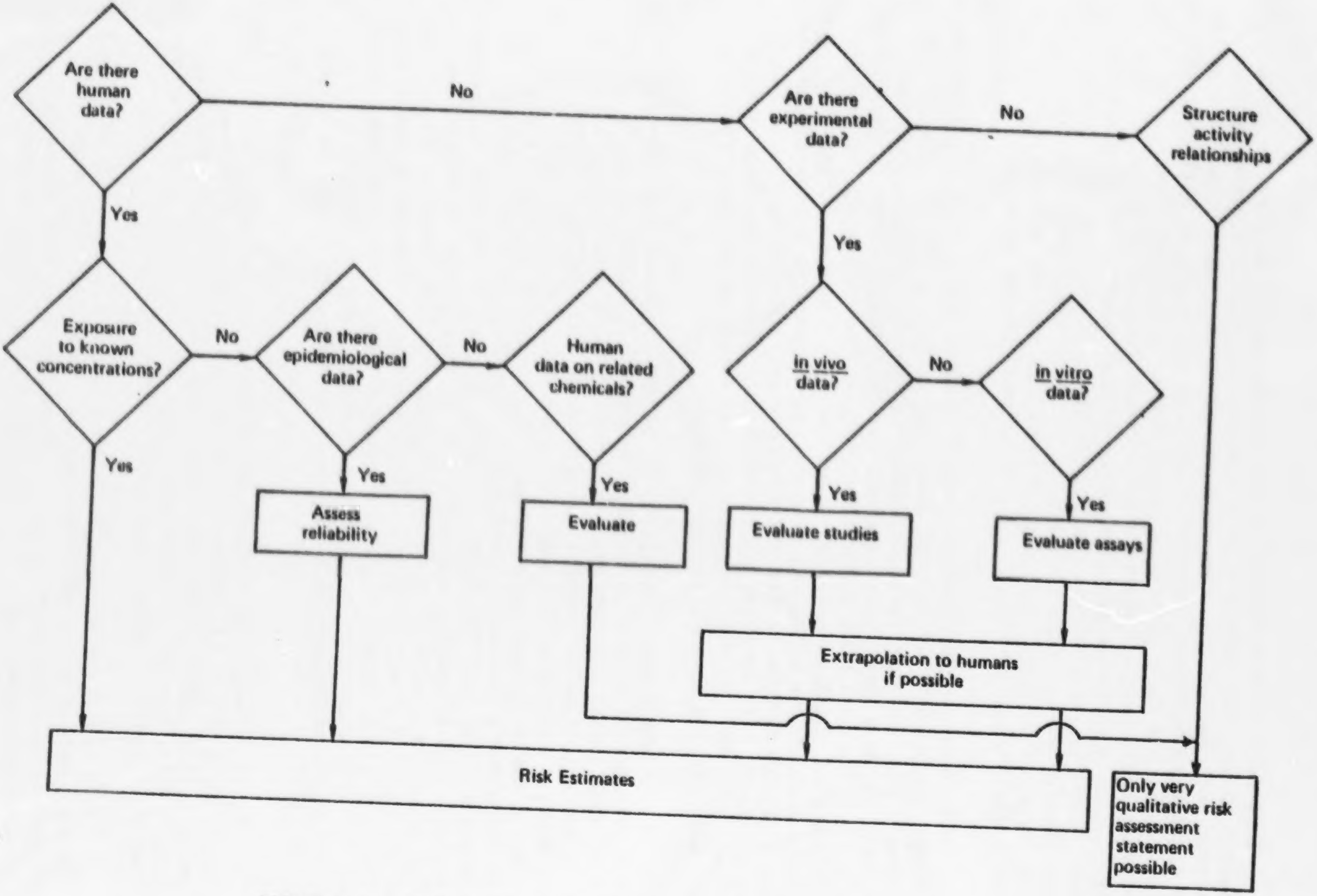
Are there human data?
No
Are there experimental data?
No
Structure activity relationships
Yes
Yes
Exposure to known concentrations?
No
Are there epidemiological data?
No
Human data on related chemicals?
in vivo data?
No
in vitro data?
Yes
Yes
Yes
Yes
Yes
Assess reliability
Evaluate
Evaluate studies
Evaluate assays
Extrapolation to humans if possible
Risk Estimates
Only very qualitative risk assessment statement possible

FIGURE 7–6 FLOW CHART FOR TERATOGENICITY RISK EVALUATION

experimental data can be examined and evaluated. High reliability and certainty is given to animal studies in vivo, with caution to extrapolation to humans as indicated above. In many cases, only qualitative estimates of risk will be possible for teratogenesis.

Fetotoxicity and Other Reproductive Effects

The interrelationship among lethal action upon the embryo, maternal toxicity, and teratogenic effect is complex and the distinction of one type of effect from another is not always clear. Until recently, reproductive hazards have not been considered in depth by scientists, industry, and regulatory agencies. A major obstacle in resolving this problem is the serious lack of clear scientific knowledge about toxic agents that affect reproduction.

The reactions of an embryo to a particular chemical depend on a number of factors: species differences involving absorption, metabolism, excretion rates, distribution and concentration of a chemical in maternal body tissues, transfer across the placenta, and the kinetics of a chemical in the embryo-placental unit. In addition, maternal adaptation to prolonged exposure and the adequate concentrations of the chemical during organogenesis, contribute to the problem of predicting effects in man on the basis of tests in other mammalian species.

Single generation studies include reproductive, teratologic, and postnatal effects resulting from exposure to a particular chemical. The study of fertility and general reproductive performance includes effects on gonadal function in both sexes, mating behavior, estrous cycle, and early stages of gestation.

In order to study the long-term effects of chronic exposure to a chemical where concentration may be a factor, the single-generation study may be extended for several generations into a multigeneration study. The toxic responses are reported as a series of indices for each generation. The fertility index or conception rate represents the percentage of matings that result in pregnancy and is affected somewhat by the fertility and libido of the male. The gestation index is an indication of the number of litters that contain live pups. It is an incomplete measure of fetal mortality unless the entire litter is stillborn. The sex ratio gives an estimate of the relative fitness of each sex and viability and weaning indices are used to measure the ability of pups to survive.

Many of the problems cited in the teratogenesis section on extrapolating experimental data from laboratory animals to man are also relevant to the analysis of the potential embryotoxic and reproductive effects of environmental agents on man. Epidemiologic data in humans are generally unavailable since exposure is frequently unsuspected or difficult to quantitate. A notable exception is the fetal alcohol syndrome.

Various forms of the pollutant may have different effects, even in a single species of experimental animals. For example, Table 7-15 gives results of a study of the effect of copper salts on pregnant golden hamsters. Copper was given intravenously on day 8 of gestation. Copper in chelated form (as citrate) was more embryopathic than uncomplexed copper (as sulfate) although the embryocidal activities were similar.

One must be very cautious in attempting to relate fetotoxic and other reproductive effects in inbred laboratory animals to similar effects in a heterogeneous human population. However, positive findings in several laboratory species would suggest the possibility of similar effects in man, particularly if the metabolic pathways of the chemical in humans and the laboratory animals are similar.

Chronic Functional Disorders

Chronic functional disorders include irreversible changes resulting from intermittent or continual exposure to low levels of a pollutant that result in detectable detriments in functional capacity (pathological, physiological, biochemical, behavioral), the ability of the organism to maintain homeostasis, or to compensate for a treatment-induced enhanced susceptibility to the deleterious effects of other environmental insults. Although all significant toxic effects are of concern, a reversible functional effect, although undesirable, would be of vastly less consequence to man than the development of an irreversible functional effect. In addition, most human exposures to environmental pollutants are typically long term exposures to low ambient concentrations, and, therefore, chronic functional effects may be the most widespread consequence of exposure to these compounds.

The ideal data for assessing the significance of a chemical as a cause of chronic human disorders would be the results of chronic administration of measured amounts of pure chemical to human subjects by the appropriate route. Since these data are not likely to be available, one must consider whatever human data are available, data from laboratory animals, and, when there are no relevant data for the chemical of interest itself, data for similar chemicals.

In all, six types of data may be used in assessing the risk of chronic functional disorders:

(1) human - chronic exposure;

(2) human - subchronic exposure;

(3) animal - chronic exposure;

(4) animal - subchronic exposure;

(5) human or animal - acute exposure;

(6) extrapolation from other chemicals.

TABLE 7-15. EXAMPLE OF PRESENTATION OF TERATOGENESIS DATA--EFFECTS OF COPPER SALTS IN HAMSTERS

Dose Level (mgCu/kg)	No. Mothers Treated	No. Gestation Sacs	No. Living Embryos (%)	No. Resorptions	No. Abnormal Embryos (%)
as Copper Sulfate					
2.13	16	210	155 (74)	55 (26)	12 (6)
4.25	3	49	7 (14)	42 (86)	4 (8)
7.5	3	30	0 (0)	22 (74)	-
10.0	2	maternicidal	-	-	-
as Copper Citrate					
0.25-1.5	13	172	143 (83)	29 (16)	4 (2)
1.8	6	81	48 (59)	33 (41)	14 (17)
2.2	8	99	65 (66)	34 (34)	35 (35)
4.0	2	maternicidal	-	-	-
Controls (demineralized water)					
0.5-1.0 ml/100g	10	125	115 (92)	10 (8)	0 (0)

Source: Perwak, J. et al. An exposure and risk assessment for copper. Final Draft Report. Contract EPA 68-01-3857. Washington, DC: Monitoring and Data Support Division, Office of Water Regulations and Standards, U.S. Environmental Protection Agency; 1980.

These types of data are listed in order of the priority that should be given to their evaluation. Figure 7-7 presents in flow chart form a general procedure for incorporating the best available data into an assessment of chronic functional effects. The least desirable pathway is the one based upon physical or chemical properties and/or structure activity relationships. Figure 7-8 is a schematic diagram showing in greater detail the evaluation process that might be followed for a pollutant to which humans are exposed by dermal contact.

In evaluating data on chronic effects, the questions one wishes to answer are as follow:

(1) What is the dose?

(2) What are the localized effects specific to the route of entry?

(3) What are the specific characteristics of route of entry, binding, absorption, distribution and elimination of this chemical?

(4) What are the chronic systemic health effects?

(5) What are the characteristics of systemic absorption, distribution and elimination of this chemical?

Although human data are the most desirable and present the most secure basis for answering these questions, these data are frequently anecdotal descriptions of chronic diseases stemming from long exposure to partly identified mixtures of chemicals. The symptoms are frequently thought to be associated with particular chemicals, but careful analysis may show that the association has not been substantiated. In addition, complex behavioral and dietary practices and the intrinsic genetic individuality of each person complicate estimates of risk associated with a particular chemical. Very few pathological states are unique and the pathognomic symptom is rare indeed. Thus, for example, demonstration of cardiomyopathy among individuals exposed to a particular chemical does not necessarily implicate that chemical in the initiation of the effect.

In the event that sufficient information is not available from chronic human exposures, one passes to the next most acceptable data groupings, subchronic exposures and acute exposures.

Data from occupational exposures to a chemical are frequently very valuable. The exposures tend to be chronic, and the chemical agent may be well identified. Documentation of these factors is very valuable. These data need to be carefully scrutinized since the occupational history of any individual may include many different exposures and other predisposing factors need to be evaluated.

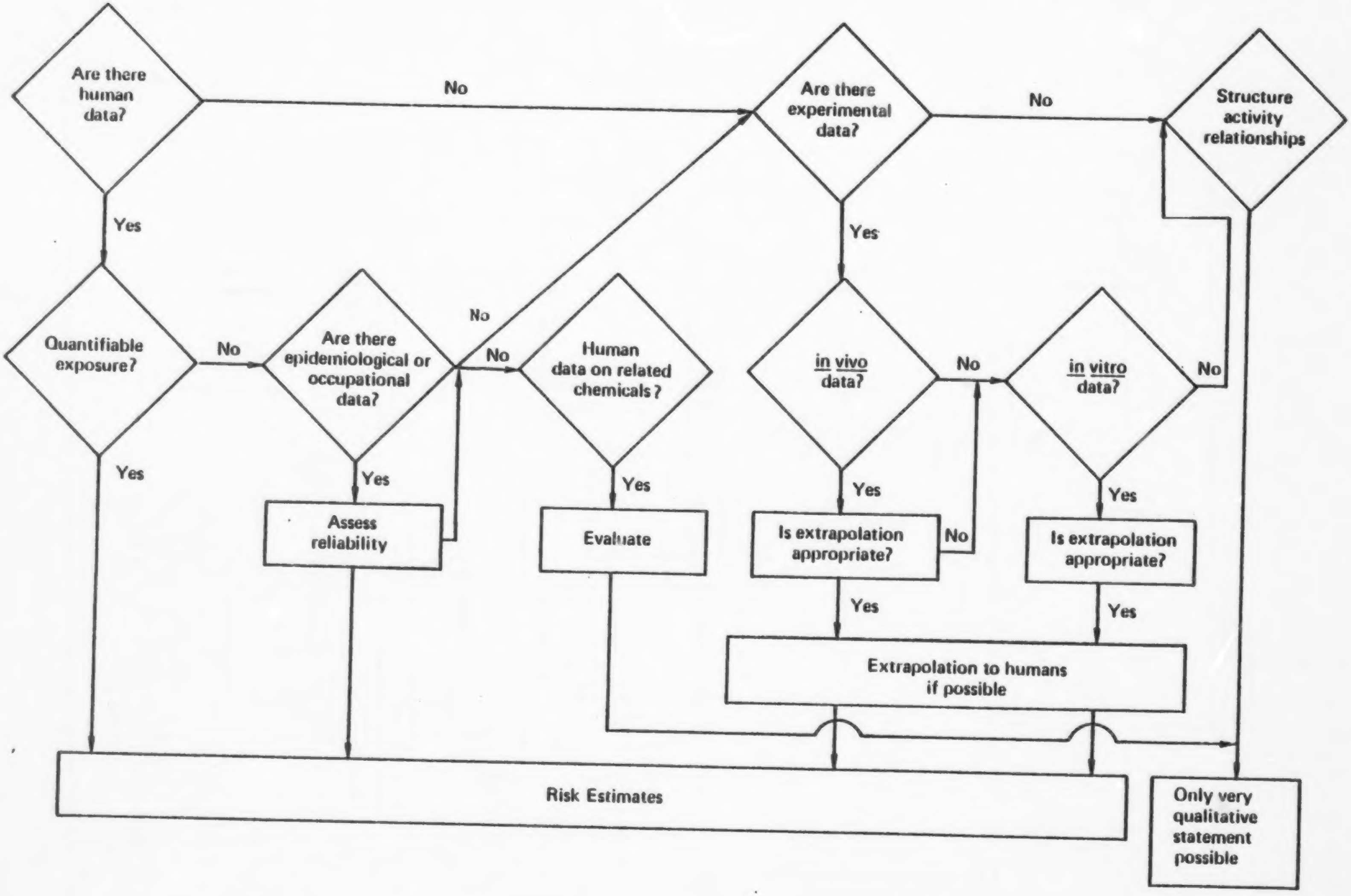
Are there human data?
No
Yes
Quantifiable exposure?
No
Yes
Are there epidemiological or occupational data?
Yes
Assess reliability
No
No
Human data on related chemicals?
Yes
Evaluate
Are there experimental data?
No
Yes
in vivo data?
No
Yes
Is extrapolation appropriate?
No
Yes
in vitro data?
No
Yes
Is extrapolation appropriate?
Yes
Structure activity relationships
Extrapolation to humans if possible
Risk Estimates
Only very qualitative statement possible

FIGURE 7–7 FLOW CHART FOR GENERAL EVALUATION OF CHRONIC FUNCTIONAL DISORDERS

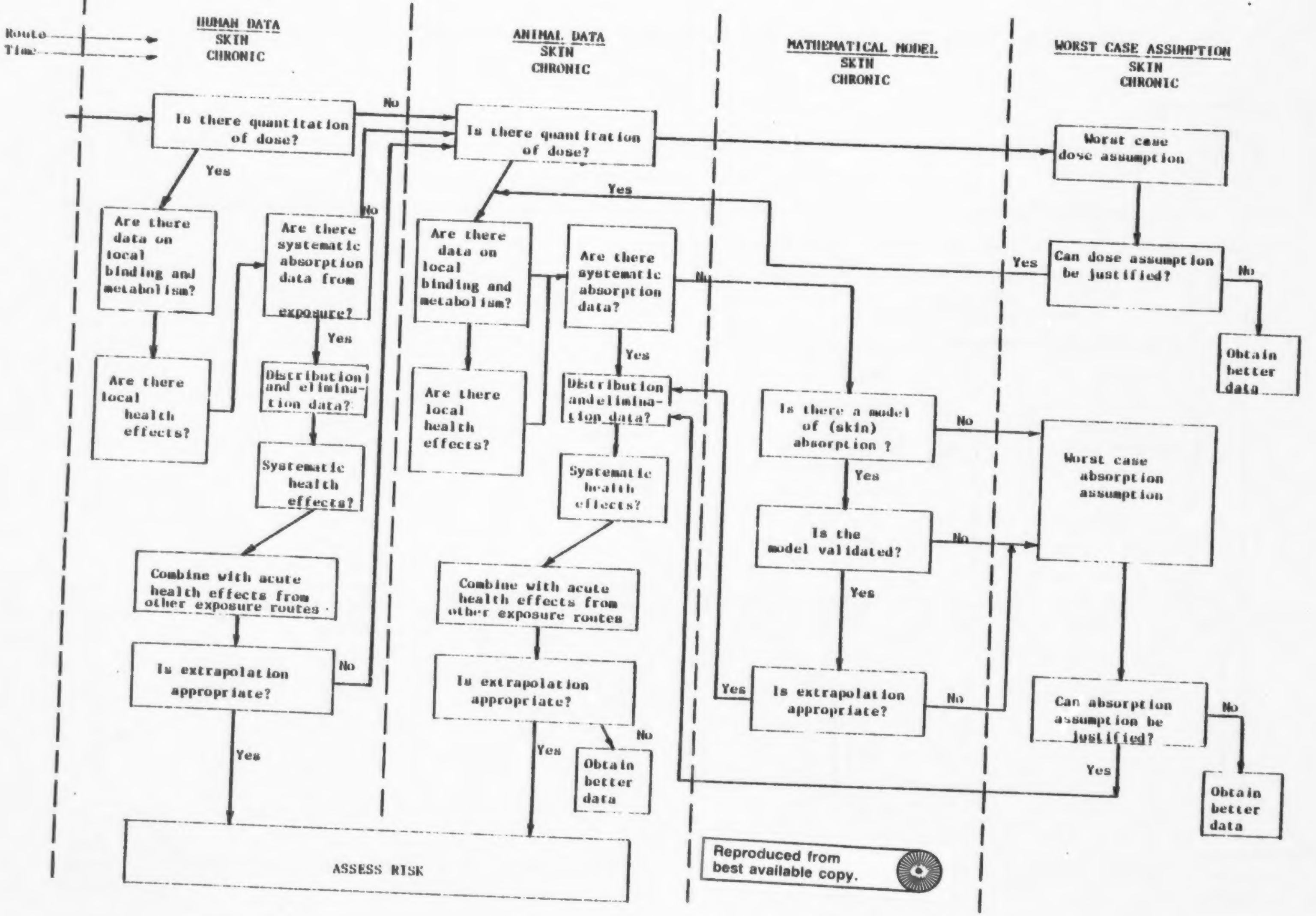
Route
Time
HUMAN DATA
SKIN
CHRONIC
ANIMAL DATA
SKIN
CHRONIC
MATHEMATICAL MODEL
SKIN
CHRONIC
WORST CASE ASSUMPTION
SKIN
CHRONIC
Is there quantitation of dose?
Yes
No
Are there data on local binding and metabolism?
Are there local health effects?
Are there systematic absorption data from exposure?
Yes
No
Distribution and elimination data?
Systematic health effects?
Combine with acute health effects from other exposure routes
Is extrapolation appropriate?
Yes
No
Is there quantitation of dose?
Yes
Are there data on local binding and metabolism?
Are there local health effects?
Are there systematic absorption data?
Yes
No
Distribution and elimination data?
Systematic health effects?
Combine with acute health effects from other exposure routes
Is extrapolation appropriate?
Yes
No
Obtain better data
ASSESS RISK
Is there a model of (skin) absorption ?
Yes
No
Is the model validated?
Yes
No
Is extrapolation appropriate?
Yes
No
Worst case dose assumption
Can dose assumption be justified?
Yes
No
Obtain better data
Worst case absorption assumption
Can absorption assumption be justified?
Yes
No
Obtain better data

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FIGURE 7-8. POSSIBLE PROTOCOL FOR EVALUATION OF DATA ON CHRONIC FUNCTIONAL DISORDERS RESULTING FROM DERMAL ABSORPTION

Human accidental exposure data are not necessarily predictive of the potential for chronic functional disorders. These exposures are not often quantitated and they are most often single, acute events. There is no certainty that the target organs that show pathological changes resulting from a single high dose exposure will be the target organs that are most often affected by a repeated lower dose. Epidemiologic studies, in general, serve to corroborate the findings of more specific animal or human work, but only infrequently define cause and effect relationships.

Frequently the available data for humans are very much less useful than would be expected. They provide descriptive clues suggesting critical organ systems but are insufficient to characterize quantitatively the relationship between exposure and effect.

Thus, animal data are frequently the only source of information available for assessing potential for chronic human impairment. Some of the problems in the use of animal data are relatively easy to predict and are the same as those mentioned previously for other health effects: extrapolation from laboratory animals to man must be accomplished by use of a scaling factor to compensate for body weight differences or surface area differences. In some cases, differences in life span present problems. Behavioral patterns may introduce difficulties in generalization between animal and human reactions to a chemical, as will subtle anatomical differences. For example, the structure of the rodent respiratory system is such that nose breathing is obligatory--in humans this is not the case. The result is a significant difference with certain chemicals in the exposure producing toxic effects due to the protection of the rodent lung by the extremely efficient nasal filtering systems. Recognizing anatomically determined differences between man and test animal requires biological sophistication and a very cautious approach to extrapolation.

The other major problem of extrapolation of animal data to humans stems from possible species differences in metabolic pathways. If it can be demonstrated that a chemical is absorbed, stored, metabolized and excreted by the same pathways in animals and man, one can expect similar toxic consequences. If the pathways or conversion rates or excretion patterns are very dissimilar, one should expect different and usually unpredictable toxic consequences, in which case, the animal studies would be an inappropriate basis for making predictions of the effect in man.

A common problem with animal data is that fairly often a response is species specific. A treatment-related response may be evident in rats and monkeys, but not in dogs, rabbits, etc. If biochemical pathway data are unavailable to explain the diversified response, the conservative approach is ordinarily espoused.

The final pathway shown in Figures 7-7 and 7-8 is evaluation of data for similar compounds. In a homologous series of chemicals, toxic effects are somewhat predictable for one member of the series based on known effects of other members of that series. In addition, some work is being pursued which would allow prediction of toxic effect by analysis of chemical functional groups (Kramer and Ford 1968). At this time, however, such models do not constitute a validated approach to prediction of human chronic functional disorders.

After the best available information has been assembled from human and animal studies, the potential for a pollutant to cause chronic effects can be estimated. The prediction of human effects from human data is obviously more reliable than that from animal data. Although the human dose may be poorly defined, one can be fairly sure that the signs are characteristic of man. Some parameters, however, are not easy to interpret. For example, changes in organ weight, change in liver enzymes in the blood, increase or decrease in a particular antibody, have all been reported at some time. It may not be possible, however, to determine whether these changes are significant precursors to organ dysfunction or whether they are meaningless, random deviations.

Other changes noted in chronic studies are reversible, that is, they will disappear after the termination of the exposures. Two types of effects tend to be reversible:

(1) exposures may temporarily modify cell function but fail to cause significant cell death; or

(2) exposures may cause significant cell death in an organ capable of regeneration.

Many cells in the body are essentially in final form (i.e., differentiated cells that cannot divide and be replaced), and in limited supply. Chemical exposure that destroys these cells, is of the greatest seriousness. Perhaps the most well known example is the heart. The loss of cardiac muscle cells is irreparable and presents serious consequences that have been well documented. Other types of cells can be easily replaced. This includes the fairly well-known replacement of nonspecialized epithelium, connective tissue, and blood cells. It also includes the more specific liver parenchymal cell. The result is that a healthy liver, which is damaged even severely by chemical insult, has a very good chance of complete recovery. Thus, in evaluating toxicity data, damage to organs that have no potential for regeneration is far more significant than damage to organs that undergo continual replacement or have a capacity to regenerate when appropriately stimulated. An assessment of the ability of organs to regenerate is shown in Table 7-16.

Another difference that determines the seriousness of chemical-induced organ damage is the degree of redundancy in that particular organ. The kidneys have sufficient structural excess to give entirely adequate function, even if 50% or more is lost. The conducting system

TABLE 7-16. TISSUE GROWTH CHARACTERISTICS: VARIOUS ANIMALS

Part I. GENERAL

	Tissue	Cell Division in Postnatal Life	Mode of Postnatal Growth	Life Span of Cells	Mechanism of Cell Replacement	Regenerative Capacity	
1	Adrenal	Mitoses, adult rat: zona capsule, 0.11%; zona glomerulosa, 0.17%; zona fasciculata, 0.11%; zona reticularis, 0.06%; total gland, 0.12%. Considerably higher figures in young rat.	Principally by cell division. Capsule may contribute.	In cortex, uncertain but phagocytosis occurs in zona reticularis.	In cortex, cell division and migration of cells from superficial to deeper layers.	In cortex, after damage, repair by cell division but limited in adult. Active regeneration follows prenatal degeneration. Mitosis very scanty in medulla; postnatal growth from cell enlargement.	1
2	Alimentary canal	Dividing cells in crypts of duodenum and ileum. In rat, make up 3% of all cells; cycle, 1.15 hr. In stomach, dividing cells at base of foveolae.	Cell division and differentiation in mucous membrane. Muscle, by combination of cell division and increase in cell size.	In small intestine, rat, 60-70% superficial epithelium shed/da; cell lives 1.57 da in duodenum, 1.35 da in ileum. Oral mucosa, rabbit, 5.1(4.5-5.7)/1000 cells [normal variation 3.6(3.6-4.0) and 7.3(6.6-7.9)]. Mitotic duration calculated as 64 min. Intermitotic period calculated as 204 hr.	Cells multiply in crypts in base of foveolae, move toward lumen and differentiate.	After removal of mucous membrane in dog's stomach, denuded area covered by growth of undifferentiated epithelium at rate of 1 mm/wk. Healing in 40 da if muscularis mucosae intact, 130 da if muscle destroyed. Brunner's glands can undergo limited regeneration. Cat's stomach: movement at 0.2-0.4 mm/hr; sudden loss of epithelium made good in a few hr.	2
3	Blood erythrocytes	Confined largely to erythroblasts in bone marrow; dividing cells in man, 1.17-1.81%.	In precursors, growth phase sharply separated from phase of hemoglobin formation.	120 da most generally accepted.	See blood. In man, 0.8% red cells replaced each da.	In rabbit, recovery from 30% blood loss, 3 wk; in rat, 7 da. In man, recovery from loss of 500 ml, 50 da.	3
4	Blood granulocytes	Confined largely to myeloblasts (1.7%) and myelocytes (0.66%) in bone marrow.	Growth stage sharply demarcated from the stages of granule formation.	Neutrophils estimated at 7-80 hr; disappear from blood of cat at rate of 861/cu mm/hr. Eosinophils, 10-14 da.		Replaced 1.5 times/da in cat.	4
5	Blood lymphocytes	In tissues of origin. Dividing cells in 3 mo rat: thymus, 0.22%; lymph nodes, 0.010%; lymph follicles in spleen, 0.016%.	Derived from reticulum cells and may be converted to other forms, but this is disputed. In dog, 25 times 10^9/kg/hr enter circulation; in cat, 35 times 10^9.	Approximately 24 hr. Removed from blood by lungs, spleen, lymph glands, skin, intestine.	See blood. Replacement in blood stream about twice a day.	Limited regeneration of lymph nodes after removal in young rabbits; mesenchyme cells form complete gland in 3-4 wk.	5
6	Blood platelets	Division of circulating platelets not described.	Evidence favors formation in marrow from cytoplasmic fragmentation of megakaryocytes.	In cat, 3-5 da; utilization at rate of 2500/cu mm blood/hr.	After loss, new formation begins in a few hr. Normal regained 3-4 da.		6
7	Brain and spinal cord	Very rare but has been recorded.	Growth of axons, myelination of fiber tracts; may not be completed until 16th yr in man.	Coextensive with normal function.	Confined to neuroglia.	Very largely confined to neuroglia; some axon [illegible] mation. Regeneration of motor axons occurs at 4 mm/da after latent period of 7 da. A large number of fibers affect rate. Preganglionic fibers[1] of cat regenerate in 16-31 da; function regained in 40 da.	7
8	Heart	Negligible in cardiac muscle.	Increase in size of muscle fibers. In rabbit, from birth to maturity, diameter of fibers increases times 4.6 (to 15μ); in man, times 2.6 (to 14μ).	Coextensive with normal function.	None.	Negligible. Hypertrophy caused by increase in size of fibers. Rabbit: normal diameter, 19.4μ; hypertrophied, 22.5μ; man, normal, 14μ; hypertrophied, 25μ.	8
9	Kidney	Rare after early postnatal life except for regeneration in rodents.	Increase in size of cells and structures. In man, from birth to maturity, diameter of glomerulus increases from 112-200μ, of proximal collecting tubules, from 18-34μ to 60-64μ. In rat, early postnatal growth partially caused by peripheral undifferentiated nephrogenic tissue, number of nephrons doubled in first two weeks of postnatal life.	Very largely coextensive with normal function.	By cell division in tubules.	True regeneration observed in rats. Hypertrophy caused by enlargement of existing elements, but increased cell division has been demonstrated after unilateral nephrectomy in the rat.	9
10	Liver	In rat, dividing cells rise from low values to 3.1% on 23rd da, then return to low values; mitotic percentage in adult albino rat, 0.005%.	In early life, considerable contribution from cell division; later, from increase in cell size.	No figure quotable.	Dividing cells persist in small numbers in adult presumably to replace cell loss.	In rat, extirpation of 2/3 regenerated in 31 da, caused by cell division in the parenchymal cells, and to a smaller extent in duct cells. Division also occurs in Kupffer cells and connective tissue cells.	10
11	Muscle, striped	Very scant and confined to nuclei. Some amitotic divisions.	Enlargement of fibers, possible splitting of fibers. In newborn, some continued formation from mesenchyme cells. Hypertrophy caused by increase of sarcoplasm in pre-existing cells.	Coextensive with normal function.	Normally none.	Protoplasmic outgrowth from pre-existing fibers in which nuclei may divide by amitosis. Outgrowth begins 3rd da after injury, progresses at 1-1.5 mm/da. New fibers 50% normal diameter in 21 da; normal diameter in 4 mo. No new formation from indifferent cells.	11
12	Ovary	Mitoses demonstrated in germinal epithelium and, during early pregnancy, granulosa and theca interna cells.	In rabbit, follicles increase in size exponentially with time, completed in 10 da, total number of oocytes in gland related to age: log(number)=4.361-0.476 log(age in da).	[illegible] of shed ova [illegible]: rabbit, 12 hr; guinea pig, 24 hr; ferret, 30 hr.		No regeneration of ova but marked regeneration activity of germinal epithelium after hormonal stimulation.	12
13	Pancreas, submaxillary		Increase of relative amount of connective tissue after birth, adult proportions reached at 14th-16th yr.			Limited amount after resection or duct ligation. Mitosis in acinar cells and duct epithelium, the latter giving rise to acinar cells and islet cells. In rat, submaxillary gland regeneration by division of acinar cells in 1st week, followed by proliferation of ducts with acini formed with terminal portions.	13
14	Parathyroid	Dividing cells in mice: 8 da, 0.01%; 18 da, 0.71%; 40 da, 0.1%.	Multiplication of clear or stem cells which differentiate into "dark" cells.			Negligible. Hypertrophy and hyperplasia in chronic nephritis.	14
15	Prostate	In rat, mitoses numerous up to 20th da, absent at 100 da.	In rat, by cell proliferation to 20th da, then by increase of cell size and diameter of acini. From 11-36 da height of cells increases from 10-14μ, and diameter acini from 41-120μ. Growth affected by hormonal activity. In man, some squamous metaplasia in newborn.		Regeneration after surgical removal very rare in man.		15
16	Skin	Occurs in varying proportions in stratum basale and spinosum. In adult mice, 2.8 dividing cells/cm length of 7μ ear section; duration of mitotic cycle, 3.5 hr. Number of divisions varies with time of da, carbohydrate metabolism, hormonal stimuli, etc. In newborn mice, 2-4% of nucleated cells in mitosis. Mitotic percentage in the planta of the rat (150g) averages 5.20% for 24 hr at 25°C.	Division of cells in deeper layers followed by differentiation.	Variable and dependent on rate of shedding of keratinized cells. Plantar epidermis cells of rat 19.1 da, of which 16.9 da are spent in basal layer and 2.2 da in stratum granulosum. Mitotic index: in corneal epithelium, rat (80-100g), 0.6%.	See [illegible]. Adjustment between cell loss and cell formation.	Re-epithelization of wounds by proliferation and migration of adjacent cells. Regeneration possible from hair follicles. Rate of healing greater in larger wounds. Growth of granulation tissue checked by epithelial overgrowth. Nails (man): growth 95μ/da (thumb). Fingernail growth 4 times toenail. Hair: length of cycle depends on thickness. Man, head, 3 yr; eyebrow, 120 da. [illegible] of rat, 35 da. Rate of growth (man) varies with site (mm/wk): head, 2.2; arm, 1.5; face, 2.1-3.5. Replacement by multiplication and differentiation of cells at bottom of hair follicles.	16
17	Testis	In albino rat, cycle of spermatogonial division, 48 [illegible]. Spermatogenic wave lasts 4 da; spermatogenic cycle takes 16 da.		Sperm survival time in man, 28-72 hr; horse, 48 hr; mouse, 13.5 hr; rabbit, 96 hr; some bats may overwinter.		Possible after slight injury. In rabbit, 1 da in abdominal cavity causes loss of spermatogenic elements, with restoration in 8 wk.	17
18	Thymus	Mitoses: adult rabbit, 0.52%; 3 mo rat, 0.22%.					18
19	Thyroid	100-125 dividing cells recorded in whole gland of guinea pig.	Weight in man: birth, 1.4g; puberty, 4g; 25 yr, 19g. Following possibilities described: new follicles by budding; proliferation of undifferentiated interfollicular cells, proliferation of cells derived from follicles.			After partial removal, hypertrophy of remainder preventable by iodine administration.	19
20	Uterus	[illegible] glands and muscle fibers, cell division of epithelial and muscle elements in addition; new muscle fibers may form from indifferent cells. Menstruation in proliferative phase mitoses in endometrium [illegible] 50% and nuclei of muscle fibers increase in size, regression of secretory phase. Denuded surface covered in 1 da by cells from remaining glands.	Pregnancy: enlargement of pre-existing epithelial cells, [illegible]			Experimental incision in mouse heals in 48 hr without scar. Smooth muscle fibers retain some power of division, new formation possible from undifferentiated connective tissue cells. Regeneration (smooth muscle) after injury limited, and fibrous scar results.	20

[1] In peripheral nerves

Part II. INCREMENTS OF WEIGHT INCREASE: MAN

Each value is derived from the weight at the end of a time period divided by the weight at the beginning of the same time period.

	Tissue	Prenatal Period[1] 0-12 wk	12-16 wk	20-24 wk	Birth to Adult
1	Brain	15	6.5	1.7	3.7
2	Heart	6.5	6.5	1.9	15
3	Kidney	35	6.7	1.6	10

	Tissue	Prenatal Period[1] 0-12 wk	12-16 wk	20-24 wk	Birth to Adult
4	Liver	17	5.5	1.8	10
5	Muscle, striped				30-40
6	Ovary				10

	Tissue	Prenatal Period[1] 0-12 wk	12-16 wk	20-24 wk	Birth to Adult
7	Pancreas	40 15	40 16	1.6	20-40
8	Pituitary	2.5	8	1.7	3-6
9	Adrenal cortex	35	5	1.7	

	Tissue	Prenatal Period[1] 0-12 wk	12-16 wk	20-24 wk	Birth to Adult
10	Thymus	400	3.7	1.9	
11	Thyroid		6.6	2.2	16
12	Uterus				20

[1] 280 da

Source: W. S. Spector (ed). Handbook of Biological Data. W. B. Saunders Co., Philadelphia 1956.

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of the heart has no excess capacity and no alternative. Again, moderate damage to the heart conducting system is likely to have more serious consequences than moderate kidney damage.

When a summary of data shown to be relevant has been assembled, it may be possible to draw conclusions concerning acceptable human exposure levels. It may also be possible to draw tentative conclusions about the seriousness or reversibility of the predicted disease state. In most cases, these conclusions will be tentative and will be the result of combinations of human anecdotal data and animal experimental data substantiated by epidemiological evidence. Predictions from chemical structure or cell culture studies are not likely to give reliable information.

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8.0 EXPOSURE AND EFFECTS--NON-HUMAN BIOTA

8.1 INTRODUCTION

Although the principal focus of the exposure and risk analyses performed for the Office of Water Regulations and Standards has been on humans. it is important to consider the exposure of fish, other aquatic organisms, and wildlife to waterborne pollutants and the adverse effects of pollutants on these species for several reasons:

(1) they may be part of the human food chain and/or of economic importance to man;

(2) they may be threatened or endangered species;

(3) because of a pollutant's critical environmental pathways or fate, its environmental impact may be on non-human rather than human receptors;

(4) assessments and regulatory recommendations of others may overlook significant environmental effects unless the hazards and risks to non-human species are considered; and

(5) they may serve as warnings or indicators of an environmental problem when media concentrations are low or non-detectable.

As in evaluating human risks, exposure and effects for other species should be considered together. Since the risk to a species is a function of both the exposure to a pollutant in a sufficient quantity or for a sufficient duration to elicit adverse effects, the risk will be small despite the potential toxicity of the pollutant. Similarly, exposure to high concentrations or quantities of a pollutant will not result in significant risk unless adverse effects can result from these exposure levels. In general, effects data for aquatic organisms and wildlife are more readily available than information on exposure. A large number of laboratory investigations have been conducted, correlations have been developed for factors such as bioaccumulation, and field or model ecosystem studies have been conducted for many pollutants and species. For most priority pollutants, the results of acute and chronic bioassays on a limited number of species are available and published in the EPA Criterion Documents.

In evaluating environmental effects, there are problems inherent in extrapolating from laboroatory data to field conditions. Unlike controlled laboratory systems, the natural environment is complex and multi-leveled, subject to both regular and irregular changes in its physical and chemical make-up. Habitats even of the same type (e.g., cold-water streams) may differ significantly in certain important variables.

Many of these variables may significantly increase or decrease the concentration of a pollutant that triggers an adverse effect. For example, differences in pH, hardness, temperature and other aspects of water chemistry may cause different effects from those detected in a simple laboratory test at the same "total" pollutant concentration.

Evaluation and quantification of exposure has its own difficulties since one must know both the population distribution and habits of the species of concern, in addition to the pollutant's environmental distribution. Materials balance and environmental pathways data provide information on pollutant concentrations and distribution. The exposure portion of the risk analysis should determine as best as possible whether there is exposure of receptors at those locations where the pollutant is present and, if so, the extent, duration, and frequency of exposure of important subpopulations. There are only limited data in the literature on the population distribution of fish, other aquatic organisms, and wildlife; their potential exposure to polluted water (drinking rates, migration patterns in and out of polluted areas) is even less well known. Therefore, in many cases, estimates or ranges of exposure will have to be first developed or postulated and then compared with scattered observations (such as fish kill reports) in order to see if they are feasible and realistic.

Although in principle all aquatic species and other biota that are exposed to polluted water should be examined in risk analyses, the effort and amount of data required generally prohibits such a detailed analysis. Therefore, the exposure and effects analysis can be concentrated on:

(1) sensitive species representative of each species category;

(2) species known to inhabit geographical regions or habitats where the pollutant is present;

(3) species for which adequate effects or distribution data exist;

(4) aquatic organisms, particularly fish.

Historical information on the long-term discharge patterns of the pollutant is important in order to examine the adaptation of resistant strains in the species present or shifts in the species composition of the local community. Information on wildlife--both exposure and effects data--is usually less common than for fish and other aquatic organisms. Also, livestock are not usually considered in this part of a risk analysis because they are rarely exposed to lethal levels of a pollutant. Instead, livestock are much more likely to concentrate pollutant levels in their tissue and the potential exposure to this accumulation is a human problem. In a similar manner, accumulation in edible aquatic species is addressed in the human exposure section, drawing upon monitoring and biological fate data. In cases where there is some understanding of the relationship between body burden and toxic effects levels, bioconcentration may be addressed in the biotic effects and exposure chapter. Otherwise it is discussed under biological fate in the environmental pathways chapter.

8.2 GOALS AND OBJECTIVES

8.2.1 Exposure Analysis

The goals of analyzing the exposure of non-human species are to determine or estimate the significant exposure routes and the extent to which aquatic organisms are exposed to pollutant concentrations in water, sediment and other organisms, and the extent to which terrestrial organisms are exposured to pollutant concentrations in soil, air, water and/or other organisms. Exposure routes include ingestion, inhalation, and dermal absorption. The extent can be defined in terms of the length of time during which populations are exposed, the geographical area in which exposure occurs, and the degree of exposure of an individual or community. The degree of exposure may be expressed as the concentrations to which the organisms are exposed or their daily intakes times and absorption efficiency.

Ideally, the results of the exposure analysis for non-human biota include:

- Identification of geographic areas with pollutant concentrations in the water or other significant media (sediment, soil) high enough to have deleterious effects on biota in order to identify, geographically, subpopulations at risk. (Monitoring data may reveal actual areas, and potential areas may be indicated by the presence of sources of pollutant releases.)
- Identification of communities or particular species--size or number, location (geographical or habitat-specific)--exposed to the pollutant.
- Evaluation of behavior patterns (e.g., migratory, reproductive, age-linked) of biota that may increase or decrease the potential for exposure.
- Identification of time-dependent patterns of pollutant availability (persistence, seasonal fluctuations, etc.) and comparison with species activity patterns.
- Evaluation of the existence of mitigating or exacerbating environmental parameters that can affect pollutant toxicity and the likelihood of their presence in areas or habitats in which environmentally significant pollutant concentrations are known or estimated.

8.2.2. Effects Analysis

The objectives of the effects portion of risk analyses for non-human biota are:

(1) Identification of those concentrations or ranges of concentrations at which a pollutant may have deleterious effects on aquatic and terrestrial organisms.

(2) Identification and evaluation of these effects--acute, chronic, reproductive--as a function of exposure levels, time, etc.

(3) Identification of factors that influence the availability and degree of impact of the pollutant on biota.

The results of the effects analysis should be compatible with the results of the exposure analysis in terms of how the levels are quantified so that the risk to aquatic and terrestrial organisms can be ascertained.

8.3 APPROACHES AND METHODS

8.3.1 Overview

In undertaking an exposure and effects analysis for non-human species, one could begin either with developing an understanding of exposure of aquatic or terrestrial organisms and then consider the effects of such exposure, or begin with effects and then consider exposure.

In the first approach, one would rely primarily on the results of the materials balance, monitoring data, and the environmental pathways analysis to identify the media and types of habitats in which exposure can occur, their geographical distribution, and the concentrations and durations associated with exposure, and then seek to establish the species or communities in those areas most likely to be exposed. Effects analysis would then focus on selected species or communities, evaluating the potential acute or chronic effects resulting from the estimated exposure levels. This approach has the advantage of limiting detailed consideration of effects to those species and populations for which exposure is anticipated or known, thereby limiting the scope and effort of the effects and analysis. The disadvantage, of course, is that one may only give detailed consideration to exposure of certain populations for which significant effects of the pollutant are not likely to occur, or to organisms for which the effects of the pollutant are unknown.

Alternatively, in beginning with effects analysis, one first identifies toxic concentration levels by examining a number of laboratory studies for a range of species and then seeks to determine the geographical areas and real situations where the sensitive species or communities may be exposed to levels sufficient to give harmful effects. This method also has advantages and disadvantages similar to those described above.

For practical reasons, it would seem appropriate to use both approaches concurrently, with the goal of quickly focusing on the exposure conditions of significance and on sensitive organisms. However, as indicated in the introduction to this section, data on the harmful effects of pollutants are more readily obtained by traditional methods of literature review and analysis, whereas exposure analysis may require a more lengthy analysis and inputs from monitoring, fate and pathways, and materials balance studies (tasks that may be proceeding concurrently). Therefore, most exposure and effects analyses for non-human biota are likely to begin with development of an understanding of potential effects and then proceed to development of understanding of exposure situations.

Figure 8-1 gives a schematic representation of the methodology used for this analysis. Note the close interaction with the other portions of the risk analysis.

8.3.2 Effects Analysis

8.3.2.1 Data Collection and Preliminary Data Review

The first step in analyzing aquatic effects is to collect readily available data on the pollutant under study. The amount and type of data readily available depends upon the pollutant being examined. If the pollutant is well known and effects have been documented, priority can be given to review articles and data compilations [such as the EPA Water Quality Criterion Documents (e.g., U.S. EPA 1980a, b)]; however, this reliance on secondary sources must be complemented by review of original publications to clear up errors and contradictions between studies that may arise. If the effects of the pollutant have not been so well studied and reviewed, then more effort must be devoted to search for published data. In addition, persons currently conducting research on the pollutant may be contacted.

Data should be collected from both laboratory studies measuring the effects of the pollutant on various aquatic organisms and field investigations or case studies documenting actual effects of the pollutant in the environment. Several information sources can be used:

- EPA sources--materials in the MDSD priority pollutant file; e.g., criterion documents, NRC reviews, fish kill data, EPA-published reports from field laboratories, etc.

- Computerized literature search in conjunction with the human effects studies using TOXLINE, Chemical Abstracts, Pollution Abstracts, Bio Abstracts, etc.

- Formal literature search--this is a second stage search, which involves retrieval of pertinent literature cited in the first sources obtained, and hand search of selected journals, e.g., Pesticide Monitoring Journal, Environmental Contamination and Toxicology, etc., which are likely to contain information on environmental pollutants.

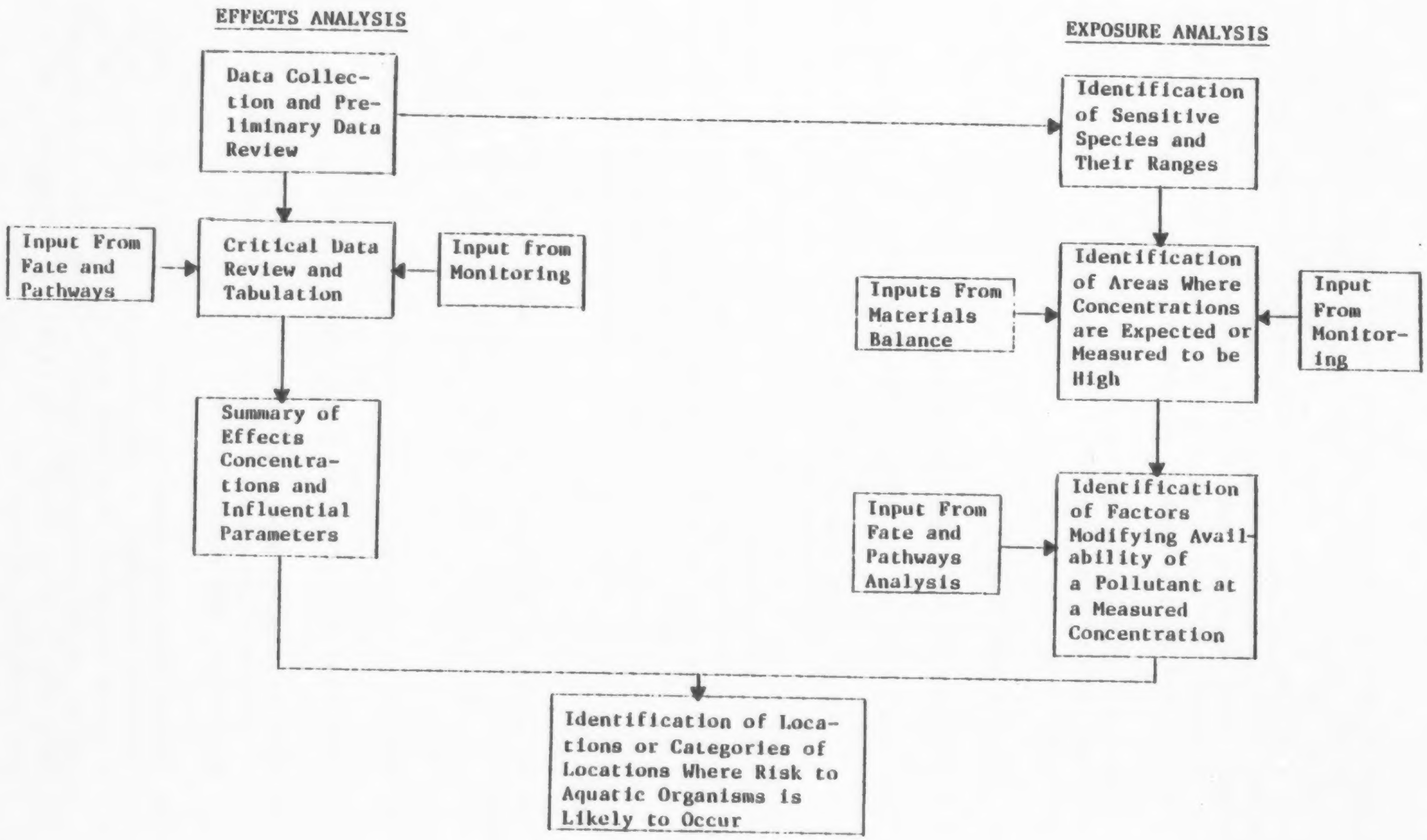
EFFECTS ANALYSIS
EXPOSURE ANALYSIS
Data Collection and Preliminary Data Review
Input From Fate and Pathways
Critical Data Review and Tabulation
Input from Monitoring
Summary of Effects Concentrations and Influential Parameters
Identification of Sensitive Species and Their Ranges
Inputs From Materials Balance
Identification of Areas Where Concentrations are Expected or Measured to be High
Input From Monitoring
Input From Fate and Pathways Analysis
Identification of Factors Modifying Availability of a Pollutant at a Measured Concentration
Identification of Locations or Categories of Locations Where Risk to Aquatic Organisms is Likely to Occur

FIGURE 8-1 FLOW CHART OF METHODOLOGY FOR EFFECTS AND EXPOSURE ANALYSIS FOR NON-HUMAN BIOTA

If information on effects of a pollutant is not available, the effects analysis must be bypassed because, in general, no method exists for estimating toxic effects. If information on a structurally similar chemical is available, it should be examined but not considered to be surrogate data for the risk analysis since the relationship between structure and toxicity is relatively unknown, making tentative any extrapolation from one chemical to another. In the absence of effects data, the research required to assess the toxicity of the pollutant (using standard aquatic species and testing procedures) should be recommended.

8.3.2.2 Critical Data Review and Tabulation

The second step of the effects methodology is to review critically the data collected and tabulate effects concentrations, in addition to consideration of the variables influencing these values.

Before the effects data are compiled, however, monitoring and fate and pathways analysis results (or preliminary results) should be reviewed. First, one should consider pollutant environmental concentration ranges available from the monitoring section to determine whether the pollutant is likely to have:

(1) no effect on aquatic organisms;

(2) some effects on certain sensitive species;

(3) effects on most species; or

(4) effects on all species, as a first approximation.

Second, a review of effects data and the initial results of fate and pathways analysis can identify critical parameters influencing availability of the pollutant to biota (e.g., pH, hardness, temperature). These considerations will help limit the scope of and define the remainder of the effects analysis.

In the data review, pollutant concentrations that have been reported to have lethal and sublethal effects on aquatic organisms are examined. Either previously compiled data or the results from the publications collected in the literature search, organized into tables that present species and effects levels in order of increasing concentration, are used. Each result must be reviewed for its scientific validity and data with serious flaws (e.g., faulty control, death of test subjects due to other causes, or lack of replication) rejected, unless no other information is available; in which case, the weakness should be highlighted.

The data are typically divided into several categories to facilitate comparison: fish and aquatic invertebrate species, freshwater and saltwater species, marine and estuarine species, lethal and sublethal effects, and chronic and acute effects. Important parameters influencing the effects at different concentrations are reported, when available.

for each experiment. These parameters include pH, temperature, water hardness, type of bioassay (static or flow-through), type of water and time of exposure. Tables 8-1, 8-2, and 8-3 are examples of effects data tabulated from risk assessments for phthalate esters, zinc, and mercury (Perwak, et al. 1981a, 1980, 1981b).

Exposure of aquatic organisms to the pollutant via gill absorption is the major focus of the effects analysis for non-human biota. However, depending on the availability of information and relevance to the pollutant of concern, several other categories of effects must be considered in this portion of the analysis:

- Toxicity of the pollutant to aquatic organisms through the route of ingestion.
- Toxicity to terrestrial species, both (1) plants through root uptake of pollutants in soil and aerial deposition and (2) animals (usually avian and mammalian wildlife species) through ingestion of contaminated biota, water or dermal contact with soil.

Data on these subjects are developed and presented in a manner similar to that for aquatic organisms.

8.3.2.3 Summary of Effects

The environmental factors that potentially affect uptake and toxicity of the pollutant are discussed either, through summarizing research indicating key factors (e.g., species groups, water hardness, duration) influencing the toxicity of the pollutant or, if that is not possible, by compilation of results of a number of separate studies in which important factors have not been controlled for. The importance of these factors in the degree of impact of the pollutant on the environment and the likelihood of their existing at sites where significant concentrations of the pollutant are found is discussed.

In many cases the information on the effects of the pollutant is insufficient to prioritize available data relative to their relevance to risk analysis. However, if possible, it is practical to consider effects in the following general order. When data are available, chronic effects (which usually occur at lower concentrations) have priority over acute effects for persistent pollutants to which long-term exposure is likely. For short-lived pollutants (e.g., highly volatile compounds) focus should be placed on acute effects; however, if releases are on a continuous basis, then chronic effects should also be considered. Effects on fish and shellfish have priority over effects on other invertebrate species because of their greater potential for ingestion by humans.

TABLE 8-1. EXAMPLE OF ACUTE EFFECTS DATA FOR FRESHWATER FISH--PHTHALATE ESTERS

Exposure Through Water

Compound	Concentration (mg/l)	Species	Effect	Conditions	Source*
Di-n-butyl phthalate	.731	Bluegill (*Lepomis macrochirus*)	96 hr. LC_{50}	17°C, static	Mayer & Sanders (1973)
	1.2	"	96 hr. LC_{50}	static	U.S. EPA (1978)
	1.3	Fathead Minnow (*Pimephales promelas*)	96 hr. LC_{50}	17°C, static	Mayer & Sanders (1973)
	2.91	Channel Catfish (*Ictalurus punctatus*)	96 hr. LC_{50}	17°C, static	Mayer & Sanders (1973)
	6.47	Rainbow Trout (*Salmo gairdneri*)	96 hr. LC_{50}	12°C, static	Mayer & Sanders (1973)
	10.0	Bluegill (*Lepomis macrochirus*)	96 hr. LC_{50}	not reported	Julin (1975) as cited in Johnson *et al.* (1974)
Di(2-ethylhexyl) phthalate	.005	Rainbow Trout (*Salmo gairdneri*)	No effect level on sac fry mortality (100 days)	10°C, flow-through	Mehrle & Mayer (1976)
	.014		Significant increase ($P < 0.05$) in sac fry mortality	10°C, flow-through	Mehrle & Mayer (1976)
	> 10.0	Fish[1]	96 hr. LC_{50}	17°C, static	Mayer & Sanders (1973)
	100.0	Bluegill (*Lepomis macrochirus*)	96 hr. LC_{50}	not reported	Julin (1975) as cited in Johnson *et al.* (1974)
Butylbenzyl phthalate	43.3	Bluegill (*Lepomis macrochirus*)	96 hr. LC_{50}	static	U.S. EPA (1978)
	445.0	Sheepshead Minnow (*Cyprinodon variegatus*)	96 hr. LC_{50}	static	U.S. EPA (1978)
Diethyl phthalate	29.6	Sheepshead Minnow (*Cyprinodon variegatus*)	96 hr. LC_{50}	static	U.S. EPA (1978)
	98.2	Bluegill (*Lepomis macrochirus*)	96 hr. LC_{50}	static	U.S. EPA (1978)
Dimethyl phthalate	49.5	Bluegill (*Lepomis macrochirus*)	96 hr. LC_{50}	static	U.S. EPA (1978)
"	58.0	Sheepshead Minnow (*Cyprinodon variegatus*)	96 hr. LC_{50}	static	U.S. EPA (1978)

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[1] Bluegill, fathead minnow, channel catfish and rainbow trout.

*See source indicated below for references.

Source: Perwak, J. *et al*. An exposure and risk assessment for phthalate esters. Final Draft Report. Contract EPA 68-01-3857. Washington, DC: Monitoring and Data Support Division, Office of Water Regulations and Standards, U.S. Environmental Protection Agency; 1981.

TABLE 8-2. EXAMPLE OF CHRONIC/SUBLETHAL DATA FOR FRESHWATER FISH--ZINC

Conc. (ppb)	Species	Compound	Hardness (mg/l)	Test Duration	Effects	Source***
5.6	Rainbow trout (*Salmo gairdneri*)	$ZnSO_4$	13-15	20 min.	Threshold avoidance level	Sprague (1968)
51	Flagfish adults (females) (*Jordanella floridae*)	$ZnSO_4$	44	100 days	Growth reduced	Spehar (1976)
106	Fathead minnow (*Pimephales promelas*)	Zn++	46	?	Effect on growth, survival or reproduction in life-cycle test**	Benoit and Halcombe*
180	Fathead minnow	$ZnSO_4$	203	10 mo.	83% reduction in egg production	Brungs (1969)
187	Chinook salmon	Zn++	22	?	Effect on growth, survival or reproduction in embryo larval test**	Chapman (1978)*
260	Rainbow trout	$ZnSO_4$	25	42 days	Chronic bioassay 6.4 mortality	Sinley *et al.* (1974)
640			330		6.9 mortality	
852	Brook trout	Zn++	44	?	Effect on growth survival, or reproduction in life-cycle test**	Holcome *et al.* (1978)*

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*As cited in EPA (1979).

**The value represents the geometric mean of the levels at which there effects are observed. In the case of embryo-larval tests the geometric mean is divided by 2 to obtain a value comparable to life-cycle studies.

***See source indicated below for references.

Source: Perwak, J. et al. An exposure and risk assessment for zinc. Final Draft Report. Contract EPA 68-01-3857. Washington, DC: Monitoring and Data Support Division, Office of Water Planning and Standards, U.S. Environmental Protection Agency; 1980.

TABLE 8-3. EXAMPLE OF LOWEST REPORT MERCURY EFFECTS DATA FOR AQUATIC ORGANISMS

Form of Mercury	Lowest Reported Effect Level (ug/l)			
	Freshwater Invertebrate	Freshwater Fish	Marine Invertebrate	Marine Fish
Inorganic	0.9[a] (Daphnia magna)	3[b] (Salvelinus fontinalis)	5[b] (Pseudocalunus minutus)	10[b] (Fundulus heteroclitus)
	5[c] (Daphnia magna)	33.0[b] (Salmo gairdneri)	3.6[c] (Mysidopsis bahia)	200[c] (Fundulus heteroclitus)
Organic	0.1[a] (Daphnia magna)	0.04[b] (Salmo gairdneri)	1.2[a] (Mysidopsis bahia)	125[a] (Fundulus heteroclitus)
		5.1[b] (Salmo gairdneri	150[c] (Gammarus duebeni)	

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[a] chronic value

[b] Sublethal effect

[c] Acute value (LC_{50})

Source: Perwak, J., et al. An exposure and risk assessment for mercury. Contract 68-01-5949. Washington, DC: Office of Water Regulations and Standards, U.S. Environmental Protection Agency; 1981.

Lethal effects and reproductive impairment effects have priority over sublethal effects--e.g., avoidance behavior and physiological changes--because of their known adverse impact on receptor populations.

To summarize the effects section, individual species, species groups, and age groups that are most sensitive to the pollutant are distinguished, along with the importance of other environmental parameters, in order to identify specific subpopulations of aquatic organisms that are likely to be at higher risk.

8.3.3 Exposure Analysis

8.3.3.1 Introduction

Analysis of the exposure of aquatic organisms is generally more qualitative than quantitative in nature. This is due to the difficulty of reliably estimating biota populations and their distribution on a national, or even regional, scale. Without this information, quantitative exposure models are not useful. As described previously, exposure analysis depends on the input of data from other portions of the risk analysis.

Effects data point out the pollutant levels with significant biological impact and, therefore, better define the boundaries of the exposure analysis for the pollutant. This can also aid in organizing monitoring data retrieval from large data bases (e.g., STORET). Effects data are also useful in the initial part of exposure analysis in identifying those species and their habitats on which to focus efforts, as suggested by results indicating most sensitive species or identifying environmental variables conducive to pollutant availability.

Monitoring data are very important to exposure analysis. Pollutant concentrations in different environmental media or good estimates of concentrations are required before effects data obtained in the laboratory can be evaluated for their relevance to natural conditions. Without knowledge of a pollutant's environmental concentrations, the risk to aquatic species cannot be estimated; effects data only satisfy one-half of the data requirements. For this reason, monitoring data should be collected with the sensitivity of non-human species in mind in order to facilitate exposure analysis. The focus can be on significant exposure pathways (e.g., surface water) and pollutant concentrations (e.g., greater than a minimum effects level).

Environmental fate and pathway information is significant in the exposure analysis when used in conjunction with monitoring data. Understanding of the pollutant's behavior in the environment can indicate the biological availability of the pollutant in environmental media to which biota are exposed. For example, if the fate data indicate a low free fraction of a pollutant at high water hardness or a tendency for adsorption, this information can be used in the qualitative interpretation of pollutant concentrations reported in monitoring programs as "total" levels, i.e., in assessing pollutant availability to and potential effects on aquatic organisms. Areas that are likely to have the environmental properties that might be conducive to pollutant availability (e.g., areas with low water hardness, low concentrations of complexing agents) can be identified through information from the fate analysis. If more specific monitoring data (e.g., dissolved or available concentrations) are available, these can be used to corroborate inferences about types of habitats with a high exposure potential.

In the absence of monitoring data, fate and materials balance information may permit estimation of ambient concentrations through the use of fate models (e.g., EXAMS, fugacity models).

Materials balance information can also be used together with monitoring data to identify geographic areas where exposure of aquatic organisms is likely to exist due to the presence of releases. Because of its general nature, it is more useful for indicating areas (regions, river basins, etc.) likely to have high pollutant concentrations relative to other comparably sized areas than for targeting specific potential problem sites.

Since the focus of the risk analysis process is often national rather than local, the monitoring data collected and used represent large areas (usually no smaller than a minor river basin). Therefore, the monitoring data are not likely to directly corroborate the fate and materials balance analyses due to differences in scale or rounding off. As a result, quantitative analysis (e.g., implementing speciation models on total metal concentration) is not possible because of requirements for site-specific input data.

Other types of information useful in analysis of non-human exposure as a confirmation of monitoring, fate, and materials balance data, include fish kill data and site-specific investigations of the effects of the pollutant in the environment. Ideally, fish kill data provide information on types of sources, locations, and temporal distribution of pollutant concentrations actually observed to have lethal effects on biota in the field. Information that would help interpret these results is usually not available. Field studies are likely to be more detailed and to measure parameters influencing the pollutant's behavior at the site of investigation but, because of the specificity of each study and the usual short time span of investigation, the generality of these studies is limited. It is unlikely there will be studies on all ecosystems or biotic communities of significance with respect to a particular pollutant. Despite the inherent weaknesses in and specificity of these data, they may serve to confirm or tie together independent pieces of information from other sections of the risk analysis.

The following sections describe the steps of the exposure analysis depicted in Figure 8-1.

8.3.3.2 Identification of Sensitive Species

If sufficient data from the effects analysis are available, the first step in exposure analysis is to identify those species most sensitive to the pollutant (e.g., salmonoids) and to determine their range (nationally distributed or locally found). In many cases, however, either data are not available for many species or the differences in sensitivity among species is not great enough (perhaps due to a very limited data base) to justify separate treatment of sensitive members. When this is true, concentrations of the pollutant in water are identified that are likely to cause deleterious effects on each group of aquatic organism (e.g., marine fish, freshwater invertebrate). Table 8-4 is an example of how these data may be organized (Scow et al. 1981a).

8.3.3.3 Identification of Areas with Expected or Measured High Concentrations

This second step is approached in one of two ways, again depending on availability of data. The first approach is to use monitoring data, for example, from the STORET data base, to determine the location of areas with concentrations equaling or exceeding the effects levels set in the preceding step. Specific locations (e.g., a particular minor river basin) or larger areas of the U.S. (the Northeast) may be identified according to the distribution pattern of the particular pollutant. Figure 8-2 (Perwak et al. 1980) is an example of one method by which monitoring data may be organized for exposure analysis. If few monitoring data are available, other information on the distribution of primary sources and usage patterns (from materials balance or environmental pathways analysis) or fish kills (see Table 8-5, Scow et al. 1981b) can be used to identify locations where high pollutant concentrations may be found.

8.3.3.4 Identification of Factors Modifying Availability

For certain pollutants, data from the environmental pathways analysis can indicate qualitatively what fraction of pollutant concentration in water is actually available to aquatic organisms. For example, for many heavy metals, factors such as hardness and pH may significantly alter the effective concentrations causing deleterious effects. Monitoring data can be better interpreted through understanding these influential variables, even in a qualitative way. The STORET data base includes the distribution of water hardness and other chemical parameters on a national basis, and these characteristics can be combined with data on the pollutant concentration distribution. As an example, Table 8-6 lists the major river basins that meet zinc concentration and hardness criteria indicating a risk to aquatic biota (Perwak et al. 1980). Since the methods with which data are aggregated regionally for each factor are not always equivalent, quantification of the relationship through techniques such as regression analysis has not been possible up to this time.

TABLE 8-4. EXAMPLE OF RANGES IN EFFECTS LEVELS FOR AQUATIC BIOTA--SILVER

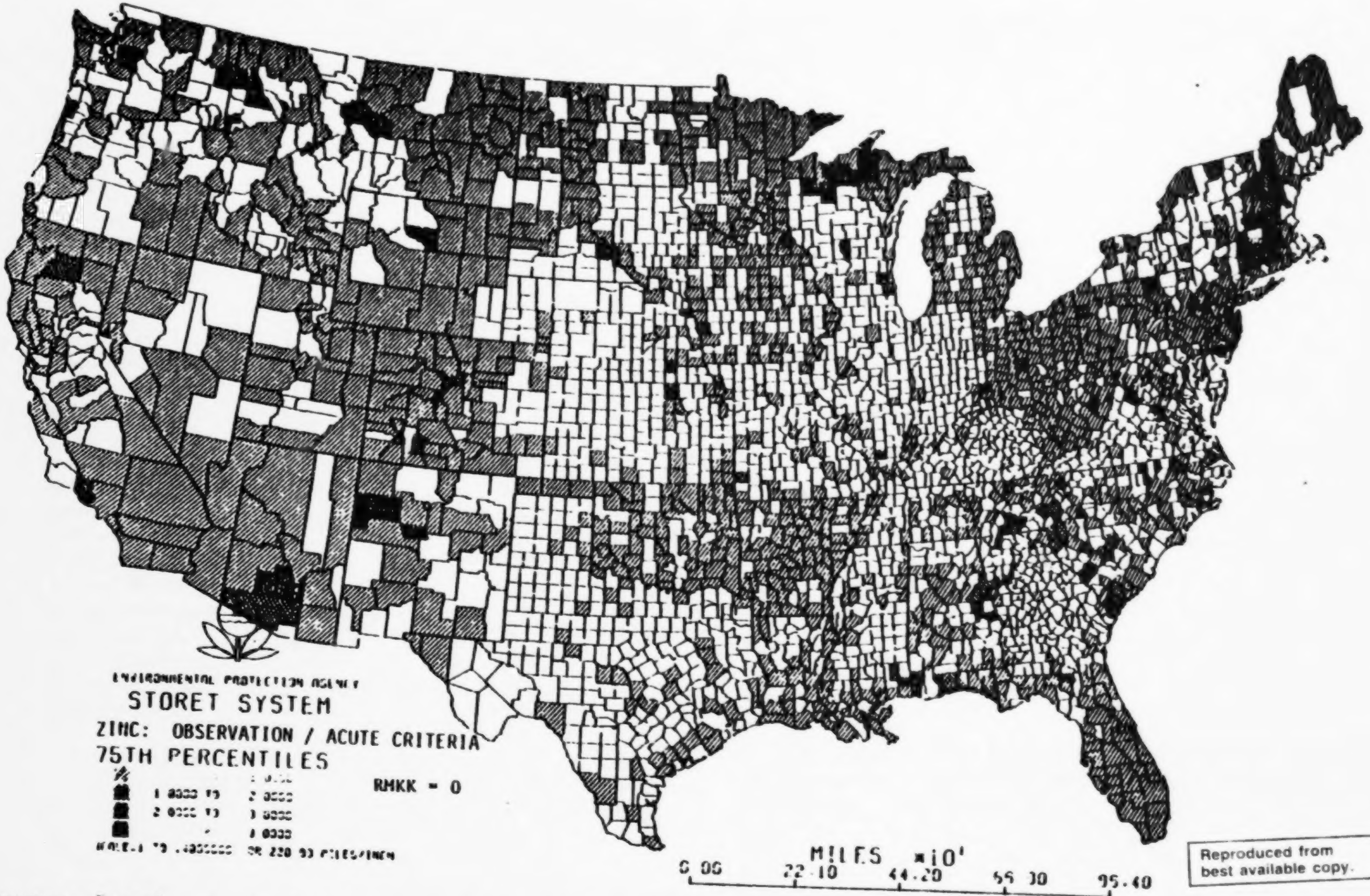
Silver Concentration	Effect
<0.1 ug/l	No effects reported for any species
0.1-1.0 ug/l	Chronic effects on most sensitive freshwater fish (mortality of trout in soft water) and invertebrates (mayfly LC_{50}). Acute effects on most sensitive marine invertebrates. (Sea urchin egg development.)
1.2 ug/l	EPA criterion to protect freshwater aquatic life at water hardness of 50 mg/l as $CaCO_3$.
2.3 ug/l (maximum at any time)	EPA criterion to protect saltwater aquatic life from acute toxicity.
1-10 ug/l	Acute effects on most sensitive freshwater vertebrates (guppy) and invertebrates (daphnia). The typical concentration range for chronic effects on freshwater vertebrates and invertebrates. Chronic effects on most sensitive and typical marine invertebrates.
13 ug/l	EPA criterion to protect freshwater aquatic life at water hardness of 200 mg/l as $CaCO_3$.
10-100 ug/l	Most reported effects levels for freshwater vertebrates and invertebrates fell within this range. Chronic effects (growth retardation) on freshwater algae. Typical range for acute effects on marine invertebrates.
100-1000 ug/l	Includes the highest concentration reported to cause acute and chronic effects on marine invertebrates. (Shrimp LC_{50} at 262 ug/l and no spawning at 103 ug/l). Sublethal effects noted for marine algae in 4 days.
>1000 ug/l	Includes the maximum reported concentration causing acute effects on freshwater invertebrates. (1400 ug/l reported for rotifer LC_{50}) and chronic effects on algae (freshwater) (toxic at 2000 ug/l).

Source: Scow, K. et al. An exposure and risk assessment for silver. Contracts EPA 68-01-5949, 6017. Washington, DC: Office of Water Regulations and Standards, U.S. Environmental Protection Agency; 1981.

TABLE 8-5. EXAMPLE OF DATA ON FISH KILLS--PHENOL

Date	Water Body	Location	Number Killed	Source
5-25-71	Roaring Brook	Glastonbury, CT	-	High phenol, Zn, Cu in fish tissues No toxics measured in water
6-8-71	Casey Fork Cr.	Mt. Vernon, IL	6,000	Wood preservation
8-6-71	Tunungwant Cr.	Bradford, PA	53,000	Discharge for chemical industry in area
8-6-71	Tunugwant Cr.	NY, near Bradford, PA	45,000	From Bradford, PA
8-6-71	Allegheny R.	Irvine Mills, NY	62,000	From Bradford, PA
1971	Ohio R.	New Martinsville, WV	5,000	Phenols from nearby chemical industry
1971	Milwaukee R.	Gratton, WI	1,500	Phenols, oil from storm sewer (?)
1972	Severn Run (Branch)	Odenton, MD	100	Phenols from plastics industry
1973	Kingsland Cr.	Lyndhurst, NY	5,000	Phenolic discharge from chemical industry
5-18-74	Hardisty Pond	Southbury, CT	550	Mixed solvents, heavy oil, and phenol
5-22-74	Banmers Pond	Naugatuck, CT	010	Asphalt and phenol
6-18-74	Red Clay Cr.	Newcastle, DE	2,000	Haveg Industry phenol spill
6-19-74	New Haven Harbor	New Haven, CT	20,000	High phenol, Al, pH, BOD, and coliform
7-29-74	Black Warrior R.	Tuscaloosa, AL	10.700	17,000-21,500 lb phenol spill by Reichhold Chemical
6-17-76	Black Rock Harbor	Bridgeport, CT	25,000	Chemical, textile, metal industries, and POTW nearby: high phenol, Cu, and Zn in fish tissues
6-22-76	Bridgeport Harbor	Bridgeport, CT	20,000	Discharges from POTW, power plant
11-17-76	Great Miami R.	Ohio	0.848	Metal and cyanide production
1976	Bear Cr.	Fairview, PA	28,000	Phenols, cyanides from agric. operations
5-10-77	Hebble Cr.	Greene Co., OH	1,000	"Government operations"
6-1-77	Sanders Branch	Hampton, SC	Total	Railway phenol spill
8-2-77	Beaverdam Cr.	Damascus, VA	150	Discharge by American Cyanamid

Source: Scow, K. et al. An exposure and risk assessment for phenol. Final Draft Report. Contract 68-01-5949. Washington, DC: Office of Water Regulations and Standards, U.S. Environmental Protection Agency; 1981.


ENVIRONMENTAL PROTECTION AGENCY
STORET SYSTEM
ZINC: OBSERVATION / ACUTE CRITERIA
75TH PERCENTILES
1.0000
1.0000 TO 2.0000
2.0000 TO 3.0000
3.0000
RMKK = 0
MILES ×10¹
0.00
22.10
44.20
66.30
95.40

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Source: Perwak, J. et al. An exposure and risk assessment for zinc. Final Draft Report. Contract EPA 68-01-3857. Washington, DC: Office of Water Regulations and Standards, U.S. Environmental Protection Agency; 1980.

FIGURE 8-2 EXAMPLE OF GRAPHIC PRESENTATION OF OVERLAP BETWEEN OBSERVED CONCENTRATION AND WATER QUALITY CRITERION FOR THE PROTECTION OF AQUATIC LIFE--ZINC

TABLE 8-6. EXAMPLE OF CONSIDERATION OF BIOAVAILABILITY OF OBSERVED CONCENTRATION OF ZINC IN SURFACE WATER

	River Basin Major/Minor Name	Zinc N	Mean Zn >120 ppb	>50% of ppb observations >120 ppb Zn	>10% of ppb observations >300 ppb Zn	>50% of hardness Measurements <50 ppm
1/9	Merrimack R.	126	*			
1/14	Presumpcot R. & Casco Bay	24	*			*
1/24	Lake Champlain	10	*	*	*	
2/8	Delaware R. - Zone 4	305	*	*	*	
2/15	Rappahannock & York Rivers	296	*	*	*	
5/2	Monongahela R.	331	*			*
5/3	Beaver R.	25	*			
5/7	Kanawha R	338	*		*	
5/13	Miami R.	86	*		*	
5/21	Ohio R., main stem & tribs	257	*			
6/3	Cuyahoga R.	21	*	*	*	
6/13	Detroit	9	*		*	
7/2	Hudson Bay, Rainy River (23/02)	5	*		*	
7/3	Upper portion, upper Mississippi R.	135	*	*	*	
7/6	Lower portion, upper Mississippi R.	189	*		*	
7/12	Mississippi, Salt Rivers	9	*		*	
7/16	Fox R.	24	*		*	
7/19	Meramec R.	42	*		*	
8/3	Menominee	50	*		*	
8/24	Green Bay, W. Shore	42	*		*	
8/49	Calumet-Burns Ditch Complex	42	*		*	
9/14	S. Central Missouri R.	70	*			
9/7	Big Sioux R.				*	
9/12	Lower Missouri R.	37	*		*	

Source: Perwak, J. et al. An exposure and risk assessment for zinc. Final Draft Report. Contract EPA 68-01-3857. Washington, DC: Office of Water Regulations and Standards, U.S. Environmental Protection Agency; 1980.

8.3.3.5 Identification of Locations in Which Risk to Aquatic Organisms is Likely to Occur

The final step in the biotic effects and exposure analysis is to summarize the results of the two sections to indicate areas where a significant exposure potential exists. Areas may be regional (e.g., the Northeast) or categorical (e.g., at the mouths of major rivers) depending on the data base and other factors discussed previously. In addition, exposure may vary temporarily if discharge patterns are seasonal, if certain age-groups of a species are more sensitive (these also vary seasonally), or if certain seasonal environmental processes (e.g., spring rains) increase the availability of a pollutant.

8.3.4 Terrestrial Effects and Exposure Analysis

Although most of the information described here is concerned with waterborne routes of exposure to priority pollutants, terrestrial systems should also be considered for those situations in which a pollutant is directly applied to plants (e.g., as a herbicide, seed fungicide) or for pollutants that are likely to be distributed on or be disposed of in the soil and expose plants through root uptake. Effects on plants, as well as those on higher members of terrestrial food chains (e.g., pheasants), should be considered when data are available. The effects and exposure analyses for these terrestrial species are usually very brief, at most indicating sites (e.g., vicinity of manufacturing plants, landfills) where exposure of terrestrial biota may occur and the range of possible effects. Discussion of environmental factors determining exposure levels (e.g., leachability of pollutant, soil pH) should be included when applicable.

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9.0 RISK CONSIDERATIONS

9.1 INTRODUCTION

In the previous sections of this report, goals and objectives, methods and approaches have been presented for evaluating the characteristics of a pollutant--the sources of its release to the environment, its pathways and distribution in the environment, and its exposure and effects on humans and other biota. Each of these components is important in its own right; yet for the regulatory agencies, as well as the public, it is essential to integrate them in order to establish, as best possible, the current or potential impact of the pollutant on man and his environment. Thus one needs to establish a "bottom line" for the analysis--how much of a problem is the pollutant, what are the risks associated with each increment in exposure to the pollutant, and how do the risks compare with those of other pollutants? The answers to these questions place risks and problems associated with the pollutant in perspective, so that they can be evaluated and acted upon, if necessary, by the parties involved.

In other research on the risks of environmental pollutants, the term "risk assessment" has been given two general interpretations. First, it has been used to connote a broad assessment of the overall risk associated with a pollutant, including risk to humans, fish and wildlife. Second, it has had a narrower meaning, namely the quantitative human health risks associated with a pollutant, often as a result of documented or estimated carcinogenicity or mutagenicity (e.g., the extrapolation of laboratory animal data on carcinogenicity to humans). In this report, the term "risk considerations" is used to signify the evaluation and integration of the information on the pollutant for the purpose of yielding an understanding of the nature and extent of risks to humans and other biota associated with the pollutant.

More specifically, the "risk considerations" portion of the risk assessment should answer the following types of questions:

- Does the pollutant cause a significant increased health risk to the general human population?
- Does the pollutant cause significant increased risks to general populations of fish, shellfish, wildlife and other aquatic species?
- What is the nature of the increased risks? Can the risks be quantified? What are the risks to the general population groups?
- Are there identifiable subpopulations based on geography, age, sex, lifestyles, etc., for whom the risks are higher than those of the general human population? What is the range of risks for different subpopulations?

- What are the key components of, or contributors to, increased risk for both general and specific subpopulations of humans and other biota?

- Are there environmental or other factors that can mitigate the extent, severity, or consequences of the risks attributed to the pollutant?

- What are the sources and environmental pathways to which significant widespread risks to humans and other biota can be attributed?

Quantitative answers to all of these questions would be desirable. Practically, this may not be possible because of the lack of data on exposure or effects of a pollutant, the uncertainties in existing data and the lack of agreement on methods to define and quantify risk. Thus only in the very best of circumstances will there be data of sufficient quantity and quality to specify the actual and potential risks associated with a specific pollutant. More likely, ranges of estimated risks will have to suffice. However, formal analysis of risk can indicate areas for additional data development, identify the areas of the greatest uncertainties, and point the direction for possible measures to reduce risk, if needed.

9.2 GOALS AND OBJECTIVES

The overall goal of this portion of a risk assessment is to develop a qualitative and/or quantitative understanding of the nature, extent, and severity of the risks imposed by a pollutant on humans, fish, wildlife, and other biota. A subsidiary goal is to establish the sources, pathways, or causal factors associated with these risks so that control actions for risk reduction can be identified and evaluated, when such are required.

For a given pollutant (or family of pollutants) specific objectives for this work include:

(1) Estimating the average health risks to the general human population, based upon average exposure and the range of health effects associated with the pollutant.

(2) Identifying those human subpopulations--on the basis of age, sex, geographic location, occupation, lifestyle, or other descriptors--that sustain greater than average risks, and estimating the extent and severity of the health risks associated with the pollutant.

(3) Estimating the average risks to general populations of fish, shellfish, other aquatic species and wildlife based upon average exposure and the range of effects associated with the pollutant.

(4) Identifying the subpopulations of fish, shellfish, other aquatic species and wildlife--by geographic location, species, habits and other descriptors--that sustain higher than average risk, and estimating the extent and severity of the risks to these sub-populations associated with the pollutant.

(5) Identifying the sources, pathways, and causal factors associated with risks for human and other species in order to allow investigation of possible methods for risk control or reduction.

(6) Presenting the information on risks in a manner that is informative and understandable to technical and non-technical audiences.

9.3 APPROACHES AND METHODS

9.3.1 General Considerations

9.3.1.1 Definitions of Risk

Risk may be defined as the potential for negative consequences of an event or activity. In the context of assessment of risk from environmental pollutants, the event or activity is the release of a pollutant into and its subsequent traverse through the environment such that humans and other biota are exposed, and the negative consequences are any adverse effects on the exposed populations. Thus, if a pollutant is believed to be harmful and if it is present in the environment, there is certainly a potential for exposure and subsequent harm; that is, some risk exists. The purpose of the risk considerations portion of risk assessments is to go beyond such a qualitative statement of potential risk, by estimating or measuring this potential.

Although the nature of adverse effects may be well understood, the key difficulty in risk estimation lies in determining the probability that adverse effects will occur. The probability is comprised of two factors:

- The likelihood that groups of organisms will be exposed to various levels of the pollutants.
- The likelihood that exposed organisms will experience adverse effects.

These two factors correspond to the two major branches of investigation described in previous sections--exposure and effects.

Analyzing the probability of adverse effects of different pollutants will present different types of problems, depending upon pollutant properties and effects. For a highly persistent substance that is present in the human diet and known to have long-term effects, the main challenge lies in estimating the likelihood of adverse effects based upon observed exposure levels. On the other hand, for a substance that is degraded rapidly and appears only in scattered locations, but is known to be an acute toxicant, the focus should be on estimating the likelihood of exposure. Therefore, the risk estimation methodology must be flexible enough to encompass these and a multitude of other situations.

For a population of susceptible organisms, risk may be expressed in several ways. One can state the probabilities that certain fractions of the population will be adversely affected (e.g., 5% chance that 9/10 will be affected, 20% chance that 1/3 will be affected). This sort of quantitative estimate is usually difficult to achieve. Alternatively, one can state the expected number that may be affected, allowing a certain margin for error to reflect uncertainties in the underlying data (e.g., 200,000 ± 50,000). Finally one can give an order-of-magnitude estimate that has no real measure of confidence attached to it (e.g., at most 5% will be affected). Each of these ways of expressing the degree of risk can be more detailed in terms of types of effects, e.g., the chance of a specific disease, premature death, extent of disability, etc.

Hence, risk estimates may be classified into three types, corresponding to decreasing level of precision with which the population at risk and the degree of risk can be characterized.

- probability distribution,
- numerical interval, and
- order of magnitude.

The level of precision of a risk estimate cannot exceed the precision of the exposure and effects data from which it is obtained. In cases where probabilistic risk estimates cannot be obtained, it may be possible to develop a range or numerical interval of risks. In other cases, lack of data may preclude any process other than the most general or comparative estimate of risk.

9.3.1.2 Overview of Evaluation Approaches

An evaluation of the risks associated with an environmental pollutant will usually consist of more than one result; it will describe the spectrum of risks identified in a variety of different cases characterized by features such as:

- nature of the adverse effect,
- subpopulations affected, and
- temporal aspects (e.g., frequency).

Often different receptor populations will be exposed in different ways over differing periods of time, and will experience different effects as a result. The spectrum of such risks must, therefore, be described to the extent permitted by the available data on exposure and effects, developed according to the methods of the preceding sections. For some pollutants, these data may not be sufficient for quantitative estimates, and consequently the risk assessment may be only qualitative. However, even with incomplete data, it is often possible to make meaningful statements about risk.

An overview of an approach for guiding the risk estimation process is shown in Figure 9-1. As shown, effects and exposure are first considered in parallel. Then, depending upon the level of precision with which effects and exposure can be quantified, the results are combined into one of four possible outputs.

For considering health effects, the first task is to review effects data for the pollutant in order to ascertain whether toxic levels can be quantified for specific toxic effects. The methods for dealing with chronic or acute effects are substantially different; they have been discussed in Section 7.0, and will be explored further below. The level of precision of the toxicity estimates will determine the attainable level of precision for the resulting risk estimates and will likely be different for each category of toxic effect.

Exposure data are also reviewed in order to ascertain whether exposure can be quantified, and to select a suitable level of precision for combining exposure with effects data.

There are four distinct possible outcomes of this procedure:

- Neither effects nor exposure are quantifiable. A qualitative indication of risk may be given if the nature of the effects, the predominant exposure routes, and populations at risk can be identified (output 4 on Figure 9-1).
- Only exposure is quantifiable. By making conservative assumptions about effects levels, a hypothetical discussion of potential risks is possible. Thus, if a risk indeed exists, one can at least identify the subpopulations that would be most severely affected (output 3 on Figure 9-1).
- Only effects are quantifiable. In this case, by postulating realistic exposure levels, one can discuss the risk that would be present under various exposure scenarios (output 1 on Figure 9-1).
- Both effects and exposure are quantifiable. This is the only output for which a detailed and quantitative assessment of risk would be possible. By combining estimates of exposure and toxicity with information about the size and distribution of the

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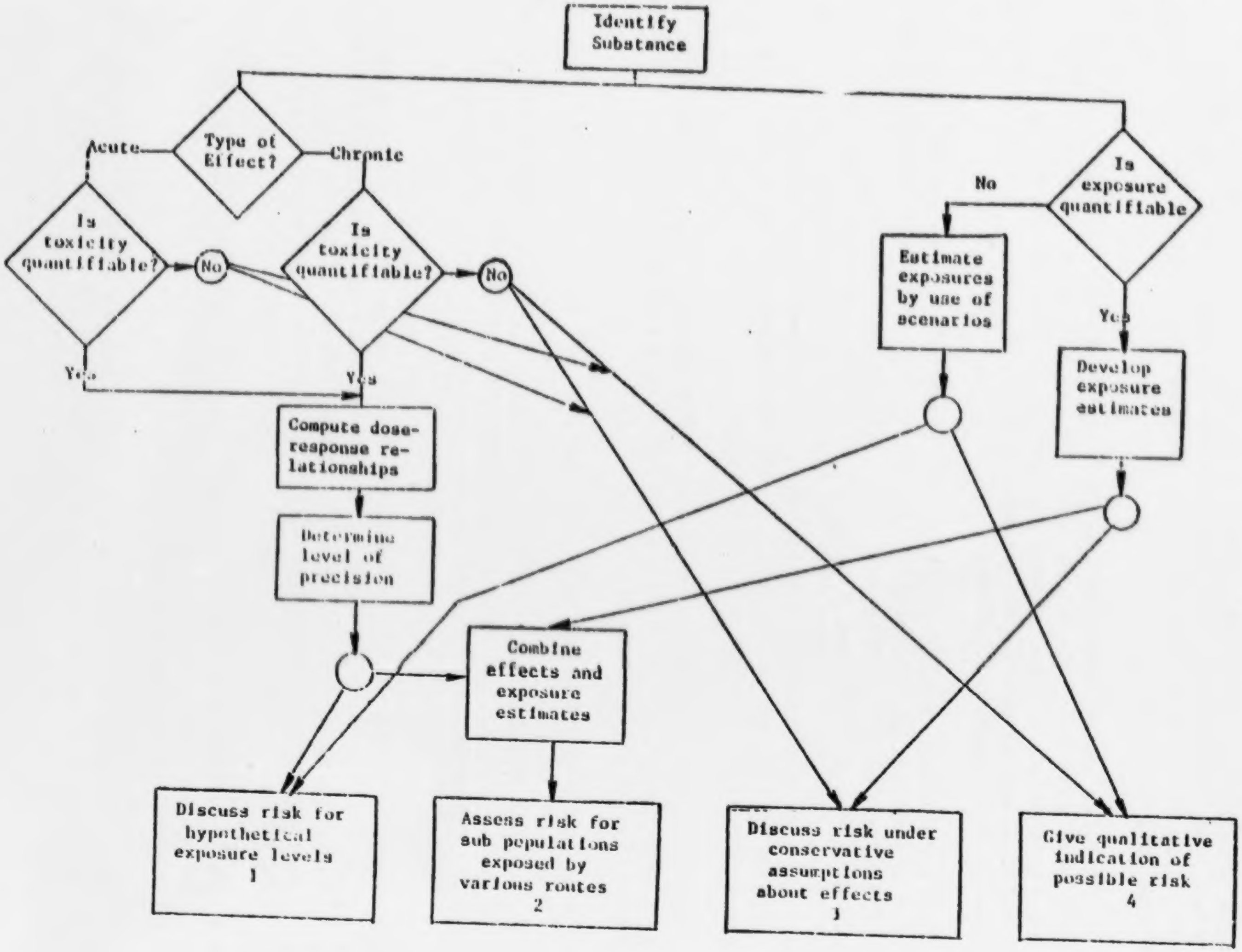
Identify Substance
Type of Effect?
Acute
Chronic
Is toxicity quantifiable?
No
Yes
Is toxicity quantifiable?
No
Yes
Is exposure quantifiable
No
Yes
Estimate exposures by use of scenarios
Develop exposure estimates
Compute dose-response relationships
Determine level of precision
Combine effects and exposure estimates
Discuss risk for hypothetical exposure levels 1
Assess risk for sub populations exposed by various routes 2
Discuss risk under conservative assumptions about effects 3
Give qualitative indication of possible risk 4

FIGURE 9-1. FLOW CHART FOR DEVELOPING RISK CONSIDERATIONS

populations at risk, one can express numerically the risks to different receptor categories, including the specification of exposure routes, geographic extent, and frequency that characterize these risks (output 2 on Figure 9-1).

Although the discussion above suggests a straightforward approach to estimation of risk according to four possible schemes, practical considerations complicate the actual risk estimation. First, some health effects may not be quantifiable in sufficient detail for numerical analysis, whereas others may be. Discrepancies may exist among data on effects or there may be a widespread distribution of effects among different subpopulations. Second, exposure may not be quantifiable in sufficient detail for numerical analysis. It may be possible to quantify exposure for certain subpopulations and not for others; or the size of various subpopulations may not be known. Thus, for any pollutant, one can expect that there are many exposure/effects combinations (potential risks) that can be considered only qualitatively, though some quantitative expression of risk may be possible for some exposure/effects combinations.

The risk estimates obtained through these procedures should be qualified by two important types of information: the assumptions incorporated into each estimate, and the degree of confidence attached to numerical estimates. Furthermore, any risk analysis should indicate what additional data are required either to improve accuracy or precision or to confirm certain assumptions.

9.3.1.3 Approaches Described in the Literature

Within the past few years, there has been considerable interest by regulators, regulated industries, and the public in methods for estimating risks, particularly the risks to human health. The setting of tolerances for pesticides in food or feed, instituted in 1947, required consideration of exposure and effects to develop safe levels of pesticide residues. The Delaney Amendment to the Pure Food and Drug Act required a different approach, by setting a zero tolerance for food additives that contained substances carcinogenic to experimental animals. In 1976, the federal government suggested procedures and guidelines for health risk assessment of suspected carcinogens (U.S. EPA 1976). Albert et al. (1977) suggested a rationale for assessment of carcinogenic risk developed by the Environmental Protection Agency. In 1977, a committee of the National Academy of Sciences dealing with safe drinking water discussed evaluation of risk of carcinogenicity and recommended the linear extrapolation approach to low doses (NAS 1977).

The Environmental Protection Agency published its approach to the development of water quality criteria, which considers quantitative and qualitative examination of both human health and environmental effects data

(U.S. EPA 1979). The Interagency Regulatory Liaison Group further discussed methods of analysis and extrapolation of health data from laboratory animals to humans (U.S. EPA 1979b). Similarly, federal agencies have suggested methods for evaluating the risks for air pollutants and hazardous waste materials (U.S. EPA 1978; U.S. EPA 1979c).

A number of health specialists have criticized the inflexible quantitative approach developed by regulatory agencies, and/or suggested other approaches to the evaluation of risk from pollutants (Kensler, 1979; Gori, 1980; Peto, 1980; Whittemore, 1980). Clearly there is a highly volatile controversy over the most desirable and appropriate approach to evaluate the health risks to man and other biota. In this methodology, several alternative approaches are recommended for consideration. Depending upon the specific nature of the pollutant and the data available on exposure and effects, one or more suitable methods may be chosen for use in each risk analysis. These methods should always be selected with a clear understanding of the associated uncertainties and assumptions. The remainder of this section discusses in greater detail the possible qualitative and quantitative approaches to risk estimation. The reader is referred to the citations given above and to the appendix of this report for additional details of quantitative risk assessment procedures.

9.3.2 Evaluation of Risk to Human Health

9.3.2.1 Overview

Earlier in this section, the goals were presented for identifying and evaluating the human health risks in a qualitative and quantitative manner for both the general and special population groups. The procedures used to evaluate risks are the same for both the general population and subpopulations; however, the exposures may be different and the resulting risk estimates may differ.

The first step in considering exposure should be to summarize the exposure of the general population and the exposure of specific subpopulations. The exposure can be summarized in terms of an average daily intake or dose for each of several different exposure routes, or the total cumulative exposure from all routes in the form of a daily intake or dose, for the average individual. Alternatively, the additional exposure to specific defined subpopulations can be presented separately as average daily intakes for each of the various exposure routes. These data will have been developed from the methods and approaches described in Section 7.0. In addition, the numbers of persons in each of the various subpopulations often can be estimated. The summary will normally include the mean or range of daily intake for the typical person, regardless of geographic location, and may include a range based upon age or sex. Maximum values or ranges should also be given for selected subpopulations whose characteristics result in greater than average intakes.

In a parallel process, human health effects of the pollutant are summarized as indicated by the available data from humans, experimental animals, and other test systems concerning the range of possible adverse effects. Finally, data are considered from supporting studies that may confirm health effects such as the results of mechanism of action or pharmacokinetic studies. To the extent that the available data are sufficient, no-observed-effect levels (NOEL) or lowest-observed-effect levels (LOEL) for different types of health effects are presented; gaps in the data are so identified. In these summaries, it is important to identify the exposure routes, the dose levels for the different responses, and the species for which the observations were made.

9.3.2.2 Qualitative Risk Analysis

The most general type of risk analysis that can be accomplished is a simple comparison of the various exposure levels with the NOEL or LOEL levels. From such a comparison, a qualitative indication can be obtained of the nature and types of risk that persons may incur. For example, if the lowest acute toxicity level for a particular functional disorder is X mg per kg body weight and the average exposure is much less than X mg per kg body weight, the risk of large-scale acute effects is low. If on the other hand, a certain subpopulation is, or can be, exposed to levels approaching or greater than X, the members of this subpopulation may be at significant risk of the acute effect. This type of qualitative comparison places the overall risks in perspective, and indicates the areas (effects and exposures) requiring additional studies or evaluations. Since one is not attempting to obtain quantitative estimates of risk with this approach, "no effects" levels in laboratory animals can be compared with human exposure levels in order to identify the potential (not probable) risks to humans.

The degree of certainty with which these comparisons can be made depends upon the precision with which effects and exposures can be characterized. For example, the effects can be better defined if they are based on human data, or experimental animal data substantiated with appropriate pharmacokinetics and mechanism of action data. *In vitro* data and data from cellular studies may also be useful in these simple comparisons in determining qualitatively whether human health effects can be anticipated.

The qualitative approach to risk assessment, relying on general comparisons of effects and exposure levels, is used when either both exposure and effects cannot be quantified (output 4 on Figure 9-1) or exposure can be quantified but not effects (output 3). If exposure cannot be quantified, some hypothetical exposure values can be developed based upon plausible scenarios, and these exposures can be compared with "no effect" or "lowest effect levels," as described above.

9.3.2.3 Semi-Quantitative Risk Analysis

When exposure to the general and specific subpopulations is known, and effects data are available with some precision (at least for animal systems), the analysis given above can be extended by consideration of margins of safety. In the development of pesticide tolerances and water quality criteria, the U.S. EPA considers the use of margins of safety to develop tolerances and criteria for chemicals that are not carcinogenic. The same approach can be used in risk analysis to obtain a relative ranking of the risks of various subpopulations to specific effects. The procedure is simply to match as best possible the NOEL or LOEL with the exposure levels (by specific route) and to develop a margin of safety by dividing the exposure level into the effects level. Ranges in exposures and ranges in effects levels can also be used in order to determine ranges in margins of safety.

The advantage of this semi-quantitative approach is that some order of prioritization can be made for risks to different subpopulations and risks of different adverse effects. For example, a margin of safety for adults for a specific effect may be 1000, but for children only 10, if the pollutant exposure is primarily a result of contamination of milk and the effects levels are based on total body burden or weight. Alternatively, the margins of safety for those who work in a particular industry may be many times less than the margins of safety for persons living near or far from the industry. Analysis of margins of safety for different exposure routes by which the same population group can be exposed may help to suggest the type of environmental controls that could reduce the exposure. In evaluating the significance of margins of safety, one must bear in mind uncertainties in the underlying data and assumptions, the accuracy and precision of the exposure levels used, and the relevance of the available effects data to the possible human exposure and effects.

Another term frequently used to establish the magnitude of risk associated with ingestion of an agent is the ADI (acceptance daily intake). The ADI is an empirically derived value that reflects a particular combination of knowledge and uncertainty concerning the relative safety of a chemical. The uncertainty factors (U.F., also called safety factors) used to calculate ADI values (NOEL/U.F. = ADI) represent the level of confidence that can be justified on the basis of the available toxicological data. Generally established guidelines for uncertainty factors are 10, 100 or 1000. When the quality and quantity of data are high, the uncertainty factor is low and when the data are inadequate or equivocal, the uncertainty factor must be larger.

In development of regulations, safety factors from less than 10 to over 10,000 are used in an attempt to reduce risks to negligible or acceptable values or to balance risks with costs. In the risk evaluation process described above, the regulating agencies are assigned the task of defining what constitutes acceptable levels of risk since the analysis attempts only to rank these risks semi-quantitatively.

Table 9-1 illustrates the expression of risk considerations by use of margins of safety (Scow et al. 1980), as an example of a semi-quantitative approach to risk assessment. The worst case scenario in the table would result in an exposure to 3.2 mg/kg per day, providing a margin of safety of 1.7 over the lowest reported no-effect level (6 mg/kg), which is for fetotoxicity. Most of the exposure in this scenario can be attributed to a spill of PCP. When the spill is excluded, the exposure would be 0.4 mg/kg per day with a margin of safety of 15. Other non-occupational exposure routes appear to have a margin of safety of at least 200.

A variant of the semi-quantitative approach may be taken for certain chemicals for which there is a significant amount of reliable epidemiological data or monitoring data and the effects in humans are well understood. For some pollutants, there may be a direct relationship between the level of the pollutant in body tissues such as adipose tissue, and acute health effects or chronic functional impairment. Also, epidemiology studies may provide information to relate exposure or daily intake of a pollutant to observed levels in body tissues. This type of information, when combined with average intakes for the general population or specific subpopulations, can show the potential risk levels in subpopulation groups. Thus the approach combines exposure information with epidemiology, bioaccumulation, and health effects studies, or monitoring data, to predict risk levels for exposed populations.

An example of applying this approach is taken from an assessment of risks associated with lead in the environment (Perwak et al., 1982a). Tables 9-2 and 9-3 present selected results of a considerable amount of research that has been done on the epidemiology of lead exposure and effects in humans. The exposure levels in human blood for various subpopulations and pathways can be compared directly with lowest reported effects levels and no effects levels for humans. As indicated by this comparison, humans appear to be at significant risk of incurring adverse effects of lead exposure, especially children exposed through ingestion of paint or inhalation and ingestion of contaminated dirt and dust and urban populations or those near industrial areas of highways with heavy vehicular traffic.

9.3.2.4 Quantitative Risk Analysis

The most quantitative and precise estimation of risk can be obtained by use of human health data from epidemiologic studies. This is often not possible because of the lack of quantified exposure data, the uncertainty in or lack of human effects data, or the confounding influence of a number of other variables affecting exposure and/or health effects.

Because of the lack of human health effects data for many chemicals, the availability of data for laboratory animals, and the continued desire to set specific levels of ambient concentrations of pollutants for the protection of human health, a great deal of emphasis has been placed in

TABLE 9-1. EXAMPLE OF RISK CONSIDERATIONS BY USE OF MARGINS OF SAFETY--PENTACHLOROPHENOL

Exposure Situation/Pathway	Exposure (mg/day)	Exposure (mg/kg/day)	Estimated Margin of Safety
Maximum Exposure			
Food	24	0.4	15
Drinking Water	0.024	0.0004	15000
Inhalation - Ambient	0.003	--	20
Dermal - Home Use - Spill	170	2.8	2.14
TOTAL	194.0	3.2	1.7
Exposure of Typical Person[b]			
Food	1.5	0.025	240
Drinking Water	0.00002	-	
Inhalation Ambient	0.003	-	
Dermal	0.003	-	
TOTAL	1.5	0.025	240
Exposure of Person Living Near Cooling Tower			
Food	1.5	0.025	240
Drinking Water	0.00002	-	
Inhalation	2	0.03	200
Dermal	0.003	-	
TOTAL	3.5	0.55	109

[a] Ratio of lowest reported no effect level (6 mg/kg for fetotoxicity) to exposure level.

[b] It is not known how "typical" these exposures are; the levels in drinking water are known to be low and numerous locations have been sampled. No monitoring data are available for air. Limited data are available for food, and the detection of PCP was not widespread.

Source: Adapted from Scow, K. et al. An exposure and risk assessment for pentachlorophenol. Final Draft Report. Contract EPA 68-01-3857. Washington, DC: Monitoring and Data Support Division, Office of Water Planning and Standards, U.S. Environmental Protection Agency; 1980.

TABLE 9-2. EXAMPLE OF ADVERSE EFFECTS SUMMARY--ADVERSE EFFECTS OF LEAD ON MAN

Adverse Effect	Lowest Reported Effect Level (μg Pb/100 ml)	No-detected-effect-Level (μg Pb/100 ml)
Carcinogenesis	--	> 40 occupational
Mutagenesis	--	40-120 occupational
Impaired Spermatogenesis	50	23-41
Fetotoxicity	30-40	--
Encephalopathy	80--children 100--adults	60--children ≥ 80--adults
Noticeable Brain Dysfunction	50-60--children	50--children
Peripheral Neuropathy	50-60	40
Nephropathy	40--children 50--adults	
Reversible		
Anemia	50-60--adults	40--children 50--adults
Elevated free erythrocyte protoporphyrin	15-20--children and women 25-30--men	20--children and women 25--men
Urinary δ-aminolevulinic acid	40	< 40
δ-aminolevulinate dehydratase	10	< 10

Source: Perwak, J. et al. An exposure and risk assessment for lead. Final Draft Report. Contracts EPA 68-01-3857 and 68-01-5949. Washington, DC: Monitoring and Data Support Division, Office of Water Regulations and Standards, U.S. Environmental Protection Agency; 1982a.

TABLE 9-3. EXAMPLE OF EPIDEMIOLOGICAL EVIDENCE OF HUMAN EXPOSURE--LEAD BLOOD LEVELS IN MAN

Location	Blood Level (µg/100 ml)	Reference*
Adults		
Rural/Urban	9-24 Most ~ 16	Bell *et al*. (1979)
Urban	18--mean (adjusted for age and smoking) Less than 5% > 30	Tepper and Levin (1972)
Rural	16--mean (adjusted for age and smoking) Less than 0.5% > 30	
Within 3.7 meters of Highway	23--mean	Daines *et al*. (1972)
Living Near a Smelter	16% >40	Landrigan *et al*. (1975)
Children		
Urban (primarily)	40,000 children detected annually > 30	
	~ 20 yearly geometric mean	Billick *et al*. (1980)
Within 30 meters of Highway	50% > 40	Caprio *et al*. (1974)
Near Smelter--Kellogg, ID--1974 (immediate vicinity)	99% > 40 60% > 60	Walter *et al*. (1980)
1975	Somewhat reduced[a]	Anonymous (1979)
1979	Almost all < 60[a], and most < 40	
El Paso, TX	70% > 40 14% > 60	Landrigan *et al*. (1975)

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[a] Reduction as a result of reduced atmospheric emissions as well as increased sanitary procedures for the workers who were apparently exposing their children to lead through their clothing.

*See source indicated below for references.

Source: Perwak, J. *et al*. An exposure and risk assessment for lead. Final Draft Report. Contracts EPA 68-01-3857 and 68-01-5949. Washington, DC: Monitoring and Data Support Division, Office of Water Regulations and Standards, U.S. Environmental Protection Agency; 1982a.

recent years on extrapolating laboratory animal test data to estimate health effects in humans and assigning environmental criteria or standards based upon this quantitative approach. As mentioned earlier, there has been a great deal of controversy over the type of laboratory animal data that should be considered, methods of extrapolation, the validity of the results, and the use of these extrapolation procedures for the development of regulatory standards. A complete discussion of these issues is beyond the scope of this risk analysis methodology document. However, since this type of quantitative analysis can be conducted where data are available, it deserves some discussion, if only to indicate how the methods can be used, and to stress precautions in their use. (Mathematical details of the application of the methods are discussed in Appendix A.)

The toxicity of a substance in a particular species can often be expressed in terms of a dose-response curve, which quantifies the likelihood or degree of a specific harmful effect occurring at various dose levels. In some cases, acute toxic doses for humans may have been identified. However, in order to obtain the dose-response relationships for sub-acute or chronic effects in humans, controlled laboratory experiments must be performed with a species of laboratory animal presumably having similar sensitivity to the substance. When data in humans are lacking, acute effects data for laboratory animals are generally easy to obtain. However, evaluation of chronic exposure at low-dose levels, corresponding to typical ambient concentrations of pollutants in the environment, requires an enormous number of experimental animals to demonstrate a statistically meaningful response frequency. Instead, a practice has evolved to perform such experiments with a moderate number of animals at high dose levels (maximum tolerated dose), and then to extrapolate the results of lower doses. The extrapolation procedure raises a number of questions.

One point of controversy is the existence of a threshold for carcinogenic and mutagenic response to a pollutant. Some argue that an organism is able to cope with low doses of a substance through metabolic processes or repair mechanisms, so that harmful effects do not appear until a certain minimum threshold , or "safe dose," has been surpassed. There is evidence to suggest that for many types of chemicals different metabolic processes occur at high dose levels than at low dose levels, and this raises questions about the validity of linear extrapolation models. Others contend that a toxic substance must be considered potentially harmful at any dose and that a "zero tolerance" level should be assumed. This issue has often been circumvented by the approach of selecting a "acceptable" risk level and determining the corresponding acceptable dose. From a practical point of view, the behavior of the dose-response curve at low doses may be an academic question, since there is unavoidable background response due to a multitude of naturally occurring toxic agents, as well as the genetic heterogeneity of human populations. Hence, for a specific substance the real issue is whether the human response to the substance significantly emerges from this general background "noise."

Another important issue is the applicability to humans of experimental data on animals. The derivation of a human dose-response curve from animal data is predicated on the assumption that a substance with demonstrated toxicity in certain laboratory animals has a probable analogous effect on man. However, the toxic effects of many substances appear to be species dependent, as a result of different metabolic patterns. Toxic effects of a chemical may differ even among strains of the same species, or for different sexes and ages. Ideally, the toxicity for man should be verified through epidemiologic studies in situations where the substance was known to be present. Even if the substance is indeed toxic to man, the issue remains of how to estimate the relative potency of the substance in man as compared with animals. The common practice is to use body weight or some power thereof to normalize the dose levels between different species. However, there remain the questions of the similarity of metabolism, bioaccumulation, and excretion of the pollutant and its pharmacokinetics within the laboratory animal and man. One must also reconcile the life span of the animal and its stages of development relative to those of man.

Finally, the issue arises of what shape to ascribe to the dose-response curve, when extrapolating from high to low doses. The simplest assumption that can be made is that the dose-response relationship is linear throughout the entire dose range. This follows from the so-called "one-hit" hypothesis, which holds that each molecule of the substance contributes equally to the likelihood of toxic effect, and hence that there is no threshold. A rival hypothesis is offered by the Mantel-Bryan method, which uses an S-shaped dose-response curve that generally yields a much lower risk when extrapolated to low doses. Other methods that consider multi-hit or multi-stage response, time to response, and repair mechanisms have also been discussed in the literature. (These methods are described in the Appendix.) In practice, the linear "one-hit" model is the easiest to apply, although it tends to give conservative results, which may overestimate toxicity. At present none of these models has been verified for specific health effects, and the use of any of them is still controversial. For extrapolation of cancer risks, the multi-stage models appear to agree best with known biological phenomena and are presently recommended bl the EPA.

If these models are used in the attempt to quantify the relationship between animal and human effects and effects levels, explicit mention should be made of the assumptions in the process. These might include:

- Comparative susceptibility of humans and experimental animals.
- Interpretation of observed effects in animals.
- Method of dose administration.
- Computational procedure for dose conversion.
- Model selected for extrapolation to low doses.

Given the present state of the art, the uncertainty associated with such assumptions cannot be quantified, except perhaps by subjective evaluation. However, it is possible to derive, in some cases, statistical confidence bounds on the dose-response estimates, based upon the size of the experiment and the number of responses. Thus, at least a part of the overall uncertainty may be expressed numerically.

When it is possible to attempt a quantitative analysis of health effects by extrapolating from laboratory animals to humans, the approach may be summarized as follows. From a careful review of the laboratory animal studies, the one or ones are selected that most closely represent the human health effects considered in terms of animal species, dose levels, exposure routes, biological and metabolic processes, confidence of data, and other variables and assumptions made earlier. Wherever possible, a variety of models--one-hit, log-probit, multi-hit, etc.--should be used to extrapolate from the high doses of the animal experiments to the low doses of the anticipated exposure levels for the general and specific human population groups. Using these methods, one can then estimate the range of risks to humans associated with exposure to environmental concentrations, using confidence levels if possible.

A quantitative analysis of the carcinogenic risks of 1,2-dichloroethane exemplifies this approach (Perwak et al. 1982b). No data were found directly relating doses of 1,2-dichloroethane to responses in humans. Because of apparent species specificity of responses and inconclusiveness of the results, studies of mutagenicity and many other toxic effects in laboratory animals could not be extrapolated to humans. The data selected for extrapolation were the NCI data that demonstrated increased alveolar/bronchial adenomas in male mice and increased mammary adenocarcinomas in female rats (NCI 1978). These data are listed in Table 9-4. Other types of carcinomas were observed in both species, such as hemangiosarcoma, but the implied dose-response relationships were not as severe.

The experimental results in Table 9-4 for both mice and rats show three animal groups: the vehicle controls (zero dose), the low-dose group, and the high-dose group. In both species the low-dose results were not statistically significant, so that the high-dose results alone were used for extrapolation to humans. The first step in this extrapolation was to calculate the equivalent human dose rate corresponding to the experimental treatment. The approach recommended by the EPA was followed, which accounts for the duration of exposure relative to the animal lifespan and normalizes the dose rate according to body surface area (U.S. EPA 1979d). This approach is conservative, in that it results in a lower equivalent human dose than would be obtained from simple multiplication of animal dose rate (mg/kg/day) by human body weight.

Whether surface area or body weight is a more appropriate normalization factor is still open to debate. The former method yields a dose rate about 6 times lower for rats, and about 14 times lower for mice. Thus, the choice of method introduces an uncertainty of rougly an order of magnitude into the risk estimates.

TABLE 9-4. EXAMPLE OF CARCINOGENICITY DATA USED FOR RISK EXTRAPOLATION OF 1,2-DICHLOROETHANE

Species Tested	Average Body Weight (kg)	Time-Weighted Average Dose (mg/kg/day)	Observed Response (%)	Observed Effects	Duration of Exposure (week)	Animal Lifespan (week)
Male mice	0.025	195	15/48 (31%)	alveolar/ bronchial adenomas	78	90
		97	1/47 (2%)			
		0 (vehicle controls)	0/20			
Female rats	0.32	95	18/50 (36%)	mammary adeno-cinomas	78	110
		47	1/50 (2%)			
		0 (vehicle controls)	0/20			

Source: Perwak, J. et al. An exposure and risk assessment for dichloroethanes. Final Draft Report. Contracts EPA 68-01-5949 and 68-01-6017. Washington, DC: Monitoring and Data Support Div., Office of Water Regulations and Standards, U.S. Environmental Protection Agency; 1982.

The actual calculation of equivalent human dose was performed as follows, assuming an average human weight of 70 kg:

$$\text{Human dose} = 70\text{ kg X animal dose X } \left(\frac{\text{animal weight}}{\text{human weight}}\right)^{\frac{1}{3}} \text{ X } \left(\frac{5}{7}\right) \text{ X } \left(\frac{\text{duration of exposure}}{\text{animal lifespan}}\right)$$

The correction factor for body surface area is the cube root of the ratio of animal to human weight, as shown by the U.S. EPA (1979d). A correction factor of 5/7 was also included since the animals were treated only on five days per week. As a result, it was concluded that:

- the dose of 195 mg/kg/day, which produced a 31% effect in male mice, was equivalent to a human dose of approximately 600 mg/day; and

- the dose of 95 mg/kg/day, which produced a 36% effect in female rats, was equivalent to a human dose of approximately 560 mg/day.

These results are roughly the same, with slightly greater potency implied by the rat experiment. Therefore, only the rat data were used in subsequent risk estimation.

Three separate extrapolation models were applied--the linear, log-probit and multi-stage models (see the appendix) using the data for female rats (i.e., 36% response at a human equivalent of 560 mg/day). The "one-hit" extrapolation is performed by simply assuming a constant increase in probability of tumor induction for each increment of dose. This leads to a gradually rising dose-response curve, which is nearly linear at sufficiently low doses. The log-probit model assumes that carcinogenic doses are log-normally distributed, resulting in an S-shaped dose-response curve with a threshold-like effect. These two models, generally speaking, tend to bound the range of risk estimates that could be obtained from other dose-response models. The one-hit model is conservative, in that it probably over-estimates the true response at low doses, whereas the log-probit model usually results in much lower risk estimates for typical human exposure levels. The multi-stage model was applied to the combined rat and mouse data. The multi-stage model generally gives dose-response estimates intermediate to the on-hit and log-probit models.

It must be noted that interpretation of the results from these three extrapolation models for assessment of human risk due to exposure to 1,2-dichloroethane is subject to a number of important qualifications and assumptions:

- Although positive carcinogenic findings exist, there have been contradictory negative findings in tests with the same species using different routes of exposure. No adequate explanation has been found for these disparate results.

- Assuming that the positive findings indeed provide a basis for extrapolation to humans, the estimation of equivalent human doses involves considerable uncertainty.

- Occurrences of human exposure to 1,2-dichloroethane are assumed to be numerous.

- The effect on rodents of chronic exposure at low doses, such as those possibly encountered in human exposure, may be deduced by extrapolating from higher gavage doses used in the NCI experiments.

- Due to inadequate understanding of the mechanisms of carcinogenesis, there is no scientific basis for selecting among several alternate dose-response models, which yield differing results.

In Table 9-5 the estimated risks of exposure to 1,2-dichloroethane obtained from these models are summarized. The expected number of cancers per million exposed population is shown for daily exposures to 1,2,-dichloroethane ranging from 1 μg to 1 mg. The gap between the estimates is large in the low-dose region; only at doses above 10 μg/day does the log-probit dose/response curve begin to rise more steeply. The dose corresponding to a per capita risk of 10^{-5} is about 100 μg/day according to the log-probit model, which is about eight times greater than the level obtained from the linear model. The multi-stage model predicts a risk intermediate between these two levels in the range of 1 μg/day to 100 μg/day.

In Table 9-6 the results from the three extrapolation models are applied to estimated average lifetime exposure of the general population and several subpopulations to 1,2-dichloroethane via ingestion and inhalation. As shown, the subpopulation drinking highly contaminated groundwater appears to be the group at highest possible risk due to waterborne exposure. Because of limited monitoring of levels in groundwater, the size of this subpopulation cannot be estimated reliably. Other uncertainties result from the availability of only limited data on residues in spices and other foods and on atmospheric concentrations in urban areas.

Thus there is a substantial range of uncertainty concerning the actual exposure levels and carcinogenic effects of 1,2-dichloroethane. However, present scientific methods and limited data availability do not permit a more definitive assessment of risk to humans resulting from environmental exposure to this compound.

9.3.3 Evaluation of Risk for Aquatic Species

Although much of the focus of the risk considerations section of an overall risk assessment is devoted to evaluating human health risks, risks to fish, other aquatic species, and wildlife should also be con-

TABLE 9-5. EXAMPLE OF ESTIMATION OF UNIT CARCINOGENIC RISK: ESTIMATED NUMBER OF EXCESS LIFETIME CANCERS PER 1,000,000 POPULATION EXPOSED TO DIFFERENT LEVELS OF 1,2-DICHLOROETHANE

Extrapolation Method	Number of Excess Lifetime Cancers Per 10^6 Population at Exposure Level[a]			
	1 μg/day	10 μg/day	100 μg/day	1000 μg/day
One-hit extrapolation	0.8	8	80	800
Log-probit extrapolation	negligible	0.1	13	690
Multi-stage model	0.5	5	50	500
Carcinogen Assessment Group	0.5	5	50	500

[a] Estimated excess lifetime cancers are given based on three different dose-response extrapolation models. The lifetime excess incidence per 1,000,000 population exposed represents the increase over the normal background incidence, assuming that an individual is continuously exposed to 1,2-dichloroethane at the indicated daily intake over their lifetime. There is considerable variation in the estimated risk due to uncertainty introduced by the use of laboratory animal data, by the conversion to equivalent human dosage, and by the application of hypothetical dose-response curves. In view of several conservative assumptions that were utilized, it is likely that these predictions overestimate the actual risk to humans.

Source: Perwak, J., et al. An exposure and risk assessment for dichloroethanes. Final Draft Report. Contracts EPA 68-01-5949 and 68-01-6017. Washington, DC: Monitoring and Data Support Division, Office of Water Regulations and Standards, U.S. Environmental Protection Agency; 1982.

TABLE 9-6. EXAMPLE OF ESTIMATION OF CARCINOGENIC RISK DUE TO ENVIRONMENTAL EXPOSURES: ESTIMATED RANGES OF CARCINOGENIC RISK TO HUMANS DUE TO 1,2-DICHLOROETHANE EXPOSURE FOR VARIOUS ROUTES OF EXPOSURE

Route	Estimated Average Lifetime Exposure (ug/day)[a]	No. Excess Estimated Lifetime Cancers (per million exposed)[b]		
		One hit	Probit	CAG
Drinking water	<2	1.6	<0.1	1
Food	~5	4	<0.1	3
Inhalation				
rural	<0.4	0.3	<0.1	0.2
urban	<0.8	0.6	<0.1	0.4
industrial	32-120	30-100	1-20	20-60
in the vicinity of production facilities	0.8-80	0.6-60	<0.1-10	0.4-40
Isolated subpopulations				
groundwater (maximum)	800	600	500	400
inhalation in industrial area	1300	1000	1000	700

[a] Data taken from Table 7-3 of the source cited below.

[b] Estimated excess lifetime cancers are given based on three different dose-response extrapolation models. The lifetime excess incidence of cancer represents the increase over the normal background incidence assuming that an individual is continuously exposed to 1,2-dichloroethane at the indicated daily intake over their lifetime. There is considerable variation in the estimated risk due to uncertainty introduced by the use of laboratory rodent data, by the conversion to equivalent human dosage, and by the application of hypothetical dose-response curves. In view of several conservative assumptions that were utilized, it is likely that these predictions overestimate the actual risk to humans.

Source: Perwak, J., et al. An exposure and risk assessment for dichloroethanes. Final Draft Report. Contracts EPA 68-01-5949 and 68-01-6017. Washington, DC: Monitoring and Data Support Division, Office of Water Regulations and Standards, U.S. Environmental Protection Agency; 1982.

sidered. In general, qualitative approaches seem to be more practicable than quantitative approaches. This is a consequence of the large number of species that might be considered, and the general lack of detailed exposure data for these individual species. Case studies or exposure scenarios seem to be a useful approach for characterizing the range of risks.

The first step in the evaluation of risk to aquatic species is to summarize information available on the exposure of different species, the locations of that exposure, and the environmental conditions that affect exposure. Some of this information may be general, in the sense that actual exposure of fish and wildlife to observed concentrations of pollutants may or may not occur; however, the situations may be described as potential exposure conditions, where it is known that both the environmental concentrations exist in the water, and fish and/or other aquatic species are known or suspected to inhabit the area in which these concentrations are found. Environmental conditions that affect exposure include factors such as rainfall, hardness of water, pH, seasonality of pollutant concentrations, salinity, etc.

The second step is to summarize data on fish and wildlife effects in terms of the most sensitive species, types of effects observed, LC_{50}'s, and/or other indicators of toxic effects, and parameters that may influence toxic effects (e.g., other pollutants, water hardness). As was the case in the human effects analysis, it should be possible to summarize no-effect level data for different species, or lowest reported effects data, as well as more commonly available values such as LC_{50}'s. In both the exposure and effects summaries, ranges of values for exposure and effects should be presented, if available, as well as the relative degree of confidence in the data.

The next step requires a qualitative comparison of the exposure and effects data. From this comparison, one can determine the species and locations in which significant adverse effects might be expected to occur. For example, if it were established that the LC_{50}'s for a particular species had values that were in the same range as environmental concentrations of pollutant in a particular location, and it were expected that species might inhabit that location, then there would be a possibility of significant risk to that species in that location. Thus the analysis becomes one of establishing the "key intersections" between exposure and effects data with regard to specific species and geographic locations. In this regard, risk considerations for fish and wildlife often tend to be more specific with respect to geographic locations than do risk considerations for human health.

The end result of this process can be a listing or summary of species, locations, exposures, and effects levels, which indicate the combinations most likely to result in high risks. In some cases, it is possible to attempt some quantitative comparisons, i.e., to determine the extent of a specific health effect on fish and wildlife by utilizing values such as LC_{50}'s and concentrations in the ambient water. As explained in the section on aquatic effects, caution must be exercised in developing these mathematical relationships because of the differences between results under laboratory conditions and field conditions. For this reason, it is important to identify those environmental factors or conditions that can influence the adverse effects.

In order to develop the risk analyses further, case studies of individual exposure/effects situations can be investigated. For example, one can pick several of the "key intersections" of exposure and effects data and determine through field interviews, discussions with local experts, examination of evidence of fishkills, or actual field sampling programs, whether there is real evidence of exposure and/or damage to the fish or wildlife population. Specific sources located in or near the area can be investigated, appropriate mathematical models of pollutant dispersion can be used to estimate concentrations of the pollutant in the water and comparisons with ambient monitoring data can be made in order to help define the potential risk for those sensitive species that inhabit the area. Environmental factors should be considered that could affect toxicity and are specific to these geographic areas. The main purpose of these case studies is to confirm the existence of significant risk to fish or wildlife species in areas in which exposure can occur and effects are anticipated. The number of case studies conducted depends upon the scope of the risk analysis and the numbers and types of locations in which exposure is expected to occur, and the nature and magnitude of the potential adverse effects.

An example of the information that can be obtained in the case study approach is given below. Analysis of the aquatic risks associated with copper in the environment, showed that LC_{50}'s for a number of sensitive species were below 100 μg/l in the laboratory (Perwak _et al_. 1980). River basin summaries (STORET) revealed that the mean levels of copper reach or exceed this level in numerous locations in the U.S. and this suggests that the potential risk to fish and invertebrates is widespread. Further examination of detailed data from individual monitoring stations in several of these river basins indicated that the mean concentrations were not representative of ambient conditions, but resulted from very elevated concentrations in a few locations. Consideration of the form of copper involved, factors favoring complexation and adsorption, and actual reports of fish kills indicated that risk exists to organisms in specific locations, but that the risk is neither as severe nor as widespread as would have been predicted from laboratory data.

The end result of risk considerations for fish and wildlife will generally be a series of summary statements indicating the locations in which adverse effects are likely to occur, the species that are likely to be affected, the environmental conditions that influence whether or not the potential effects actually occur, and the results of case studies to confirm or establish the magnitude of the potential problems. In addition, areas for further investigation should be identified.

9.3.4 Summary of Risk Considerations

The approaches described above can provide specific information on the nature and extent of the risks to both general and specific human subpopulations and to fish and other aquatic biota. Depending upon the type and level of data available concerning exposure and effects, specific conclusions may be drawn giving the ranges of risks and the degree of precision associated with these risks. In some cases, only qualitative aspects of risks can be presented; in others, quantitative information may be appropriate.

In either case, the overall risk posed by the pollutant should be portrayed so that regulators and the public can visualize whether or not significant problems are expected to occur. A number of methods of presenting this overall summary of risks are possible: tables or charts showing specific risks to humans and other species, charts or graphs showing the relative risk associated with different effects, etc. An approach that has the potential for effectively summarizing the results of risk considerations is to prepare a graphic presentation of exposure and effects in terms of the same variable and to indicate the areas in which the combinations of exposure situations and effects levels can present significant risk. This approach could be followed for both human health effects and effects on fish and aquatic species and could be specific to a particular type of effect, type of exposure, or other characteristics.

One method of presentation is to plot the relative frequency of exposure in terms of concentration or average daily intake, the frequency being defined in general terms such as "usual," "frequently," "occasional," "rare exposure." On the same graph, one could plot the likelihood of various toxic effects at levels such as LC_{50} for various species. The intersection of the exposure and effects curves, or more precisely the area bounded by the intersection, would indicate the areas of significant potential risk.

As an example of this type of presentation, Figure 9-3 shows a diagrammatic plot of the relative frequencies (ordinate) of both aquatic exposure levels and reported effects levels in terms of the surface water concentrations of arsenic (abscissa) (Scow et al. 1982). Surface water concentrations of 1 mg/l are rarely observed. The shading indicates the approximate degree of uncertainty associated with the data points used. The area under the intersection of the curves represents the region of potential risk where the observed water concentrations have values that exceed reported adverse effects levels.

Though such a plot of exposure and effects frequencies can be a useful conceptual tool, its interpretation must be made in light of the representativeness of the monitoring data base, the validity of generalizing from the available toxicological data (number of species tested, chronic versus acute effects), and other factors such as bioavailability.

If sufficient data are available concerning effects and exposure levels for humans, a similar plot could be used to summarize the likelihood of significant potential risk.

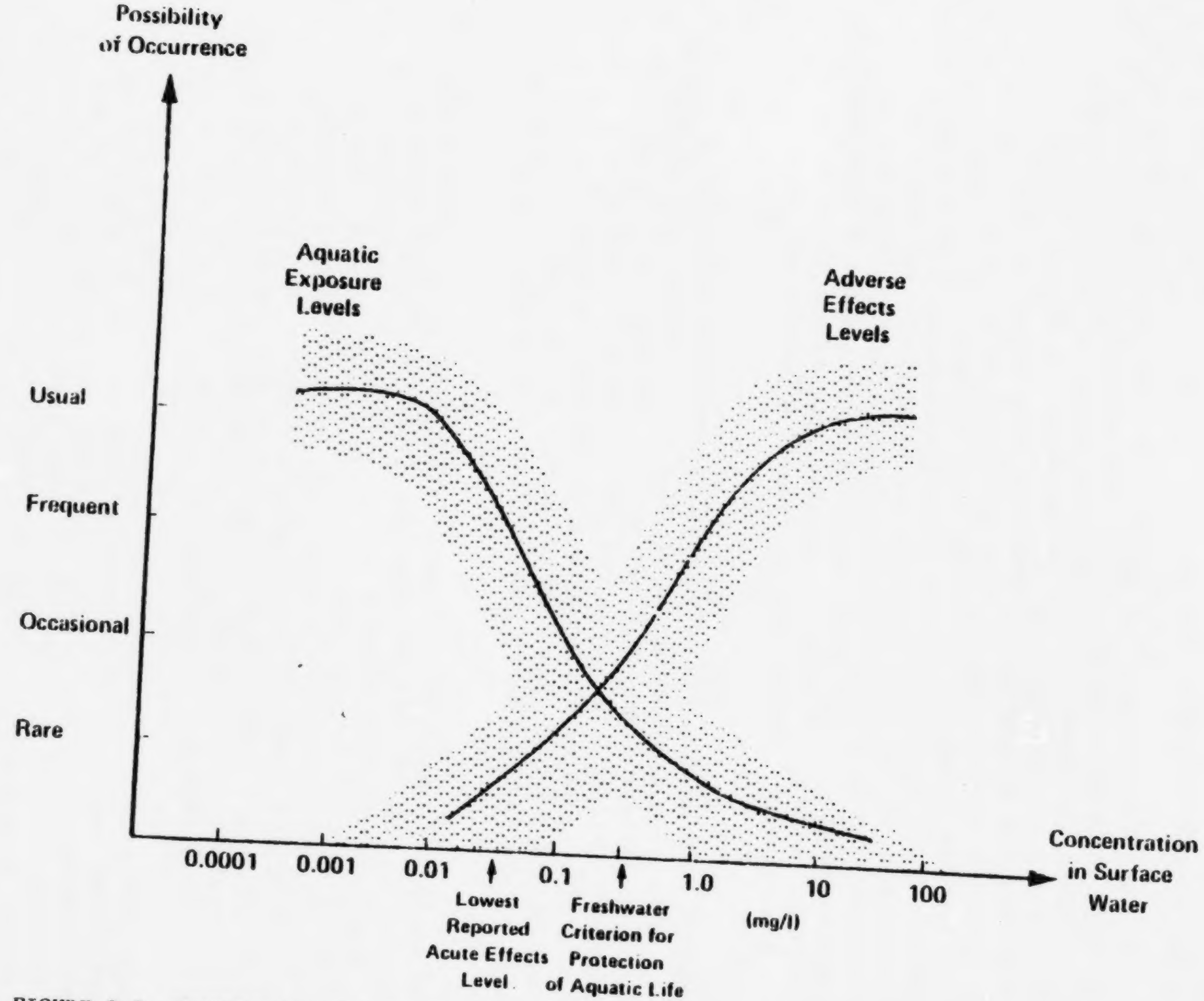

FIGURE 9-2 EXAMPLE OF RISK CONSIDERATIONS SUMMARY FOR AQUATIC BIOTA--ARSENIC EXPOSURE AND TOXICITY TO AQUATIC ORGANISMS

Source: Scow, K., et al. An exposure and risk assessment for arsenic. Final Draft Report. Contract 68-01- 6160, 6017. Washington DC: Monitoring and Data Support Division, Office of Water Regulations and Standards, U.S. Environmental Protection Agency, 1982.

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10. BIBLIOGRAPHY OF REFERENCE MATERIALS FOR USE IN EXPOSURE AND RISK ASSESSMENTS

10.1 INTRODUCTION

The following bibliography is intended to provide an initial means of identifying reference materials for use in conducting exposure and risk assessments for environmental pollutants. The bibliography is organized according to the following six topical areas of investigation:

- Materials Balance
- Environmental Pathways and Fate
- Monitoring Data and Environmental Distribution
- Human Exposure and Effects
- Exposure and Effects--Non-Human Biota
- Risk Estimation

10.2 MATERIALS BALANCE

Abstracts and Searches

Applied Science and Technology Index
Bibliographies from U.S. Bureau of Mines
Chemical Abstracts
Engineering Index
Environmental Abstracts
Metals Abstracts
NTISearch
Pollution Abstracts

Industry and Consumer Associations

American Chemical Society
American Institute of Chemical Engineers
American Institute of Industrial Engineers
American Institute of Mining, Metallurgical and Petroleum Engineers
American Iron and Steel Institute
American Paper Institute
American Petroleum Institute
American Public Works Association
American Society of Sanitary Engineers
Association of Home Appliance Manufacturers
Chemical Manufacturers Association
Environmental Defense Fund
Environmental Information Center
Gas Appliance Manufacturers Association
Glass Packing Institute
National Agricultural Chemicals Association
National Ash Association
National Association of Recycling Industries
National Family Option
National Association of Manufacturers
National Lime Association
National Solid Waste Management Association
Natural Resources Defense Council
Society of Manufacturing Engineers
Society of Mining Engineers
Society of Plastic Engineers
Synthetic Organic Chemicals Manufacturers Association
The Fertilizer Institute
Water and Wastewater Equipment Manufacturers Association
Zinc Institute

Periodicals

- Agricultural Chemicals
- AIChE Journal
- American Dyestuff Reporter
- American Paint Journal
- American Paper Industry
- Automotibe Engineering
- Beverage Industry
- Chemical and Engineering News
- Chemical and Metallurgical Engineering
- Chemical and Petroleum Engineering
- Chemical Engineering (Chemical Engineering Equipment Buyers Guide)
- Chemical Engineering Progress
- Chemical Marketing Reporter
- Chemical Processing
- Chemical Week
- Chemtech
- Coal Age
- Coal Mining and Processing
- Engineering and Mining Journal
- Food Engineering
- Food Industry
- Industrial Wastes
- Journal of the American Water Works Association
- Journal of the Air Pollution Control Association
- Journal of the Water Pollution Control Federation
- Machine Design
- Mining Engineer
- Modern Packaging
- Modern Plastics
- Oil and Gas Journal
- Packaging Design
- Pit and Quarry
- Plant Engineering
- Plastics Engineering
- Plastics Technology
- Plastics World
- Process Engineering
- Pulp and Paper
- Rubber Age
- Solid Waste Report
- Solid Wastes Management
- TAPPI
- Textile Worlds
- Water and Sewage Works
- Water and Wastes Digest
- Water and Wastes Engineering

Books

Census of Manufacturers, U.S. Dept. of Commerce, Washington, DC

U.S. Geological Survey Yearbook, U.S.G.S., Washington, DC

Mineral Facts and Problems, U.S. Bureau of Mines, Washington, DC

SME Mining Engineering Handbook, I.A. Given (ed.), AIME, NY

Chemical Process Industry, R. Shreve and J. Brink, McGraw-Hill, NY

Unit Operations of Chemical Engineering, W. McCabe and J. Smith, McGraw-Hill, NY

Metal Bulletin Handbook, R. Packard (ed.), Metal Bulletin Ltd., London

Metal Statistics, P. Cere (ed.), Fairchild Publications, NY

Minerals Yearbook, U.S. Dept. of Interior, Bureau of Mines, Washington, DC

Mining Engineer's Handbook, R. Peele (ed.), John Wiley and Sons, NY

Oil and Gas International Yearbook, P. Jenkins (ed.), Business Enterprises, London

Petroleum Processing Handbook, W.F. Bland and R.L. Davidson (eds.), McGraw-Hill, NY

Chemical Regulation Reporter, The Bureau of National Affairs, Washington, DC

Chemical Engineering Practice, H.W. Cremer and T. Davis (eds.) Butterworths Scientific Publications, London

Moody's Industrial Manual, Moody's Investors Service, NY

Encylcopedia of Chemical Technology, R.E. Kirk and D.F. Ohmer, Interscience Encyclopedia, Indc. NY

The Encyclopedia of Chemistry, C.A. Hampel and G.G. Hawley (eds.), Van Nostrand Reinhold Co., NY

Directory of Chemical Producers, U.S.A., Chemical Information Services, Stanford Research Institute, Menlo Park, CA

Chemical Sources, U.S.A., Directories Publishing Co., Fleming, NJ

Manufacturing Processes Dictionary, H.R. Clauser (ed.) Technomic Publishing Co., Westport, CN

Industrial Product Directory, Cahness Publications, Stamford

SOCMA Handbook, American Chemical Society, NY

Rare Metals Extraction by Chemical Engineering Techniques, W.D. Jamrock, Pergamon, NY

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10.3 FATE AND PATHWAYS ANALYSIS

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Advances in Agronomy
Advances in Applied Microbiology
Advances in Chemistry Series
American Chemical Society Symposium Series
American Journal of Botany
Analytical Chemistry
Applied and Environmental Microbiology
Archives of Environmental Contamination and Toxicology
Atmospheric Environment
Biochemistry
Bulletin of Environmental Contamination and Toxicology
Canadian Journal of Chemistry
Canadian Journal of Microbiology
Chenosphere
Chemical Engineering News
Endeavor
Environmental Health and Pollution Control
Environmental Health Perspectives
Environmental Pollution
Environmental Science and Technology
Estuarine and Coastal Marine Science
Journal Agricultural Food Chemistry
Journal of Air Pollution Control Association
Journal of Association Off. Anal. Chem.
Journal of Environmental Quality
Journal of the American Chemical Society
Journal of Water Pollution Control Federation
Marine Chemistry
Marine Pollution Bulletin
National Academy of Science (NAS) documents
Nature
Pesticide Monitoring Journal
Proceedings of the American Society of Horticultural Science
Proceedings of the Industrial Waste Conference (Purdue University Engineering Bulletin)
Proceedings of the Royal Society of London
Science
Soil Biology and Biochemistry
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Water Pollution Abstracts
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Data Bases

Environmental Contaminant Monitoring Program - U.S.D.I.

Pesticide Soils Monitoring Program - U.S. EPA

NASQAN - National Stream Quality Accounting Network, USGS

SAROAD - Storage and Retrieval of Aerometric Data, U.S. EPA Research Triangle Park

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10.5 HUMAN EXPOSURE AND EFFECTS

Computer-Based Toxicological Information Services

Database	Accessible Through	Database Content
CANCERLIT	National Library of Medicine	All aspects of cancer
CANCER PROJ	National Library of Medicine	Ongoing cancer research projects for most recent 3 years
EMIC	Department of Energy	Chemical mutagenesis
ETIC	Department of Energy	Chemical teratogenesis
EXCERPTA MEDICA	Lockeed's DIALOG Service	Human medicine and related disciplines
MEDLINE	National Library of Medicine	International biomedical literature
NTIS	Lockheed's DIALOG Service	Government-sponsored research plus analyses prepared by federal agencies or their contractors/grantees
RTECS	National Library of Medicine	Acute toxicity, eye/skin irritation, recommended exposure levels
TDB	National Library of Medicine	Chemical, pharmacologic, and toxicological data extracted from 80 standard reference textbooks, monographs
TOXLINE/TOXBACK	National Library of Medicine	Human and animal toxicity, effects of environmental chemical pollutants published within or prior to the last 5 years

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U.S. Environmental Protection Agency (U.S. EPA). Water quality criteria documents availability. Federal Register 45(231):79318-79384; November 28, 1980.

10.6 EFFECTS AND EXPOSURE--NON-HUMAN BIOTA

Periodicals

Archives of Environmental Contamination and Toxicology
Biological Bulletin
Bulletin of Environmental Contamination and Toxicology
Bulletin of the Japanese Society of Scientific Fisheries
Comparative Biochemistry and Physiology
Ecology
Environmental Pollution
Fishery Bulletin
Hydrobiologia
Journal of Experimental Marine Biology and Ecology
Journal of Fish Biology
Journal of Fisheries Research Board of Canada
Journal of Great Lakes Research
Journal of Invertebrate Pathology
Journal of Marine Biological Association
Journal of Zoology
Marine Biology
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APPENDIX A. MATHEMATICAL DETAILS OF RISK CALCULATIONS

A.1 INTRODUCTION

In rare instances, epidemiological studies provide direct information about the adverse effects of a substance to humans. However, even in these instances, the actual exposure intensity and duration that was responsible for these effects may be difficult to quantify. Consequently, most risk estimates for humans are based upon laboratory studies with experimental animals. It is preferable to base an estimate upon several studies with different species, in which case a range of potency may be established for the pollutant in question. Wherever possible, confidence limits and measures of statistical significance should be introduced to qualify these results. Even in a single experiment, different interpretations of the data may lead to uncertainty about the response. Further, the extrapolation from responses in laboratory animals administered high doses to the low doses characteristics of most human exposure to environment pollutants is necessarily an uncertain process. Hence several different methods should be used to establish the range of potential risk.

A dose-response curve can be defined as a relationship between the amount or rate of the chemical administered and the probability of the subject experiencing an adverse effect at that dose. Hence, the curve is a cumulative probability distribution function and should increase from zero to one, assuming that higher doses are increasingly more toxic.

The estimation of risk on the basis of experimental data involves the selection of a hypothetical dose-response curve, and the fitting of the parameters of this curve to the data. Although ideally algorithms would exist for calculations of risk due to all types of health hazards, at the present time the only effect for which a substantial body of theory exists is carcinogenesis. Three different types of dose-response models for assessing cancer risk are described in the following sections.

- The linear non-threshold model (Chand and Hoel 1974, Cornfield 1977, NAS 1977) is based upon the "one-hit" principle, which asserts that each molecule of the substance has an equal probability of producing a specific effect. The resulting dose-response curve is exponential, and is approximated by a linear curve in the low-dose regions. This method tends to produce "upper bound" risk estimates, which probably exceed the actual risk to humans.

- The Mantel-Bryan (log-probit) model (Bliss 1934, Mantel *et al.* 1971, Mantel and Bryan 1961) assumes that the susceptibility of receptor organisms is normally distributed with respect to the log of the dose. Hence the cumulative distribution of response is the integral of a log-normal density function. The resulting dose-response curve has an S-shape, and usually yields lower estimates of risk because of the implied threshold effect.

- The multi-stage model has been independently developed by several investigators (Armitage and Doll 1961, Crump et al. 1976, Crump et al. 1977, Hartley and Sielken 1977) and generalizes the linear one-hit model to allow polynomial functions of dose and time. It often reduces to a linear model in the low-dose region, but provides a better fit when the data indicate that there is a threshold effect.

These three methods and their application are discussed in greater detail below.

A.2 HUMAN EQUIVALENT DOSES

The calculation of the equivalent human dose for extrapolation of animal data can usually be accomplished by simply multiplying the human weight (70 kg) by the animal dose expressed in mg/kg per day. To cover situations in which doses are expressed in different units, a procedure was developed to compute equivalent human doses for any experimental situation. The following formulae require knowledge of the weights, dietary intakes, and respiration rates of the experimental animals.

Let D_H, D_A denote human and animal doses respectively,

W_H, W_A denote human and animal weights (kg),

I_H, I_A denote dietary intakes (kg/day), and

R_H, R_A denote respiration rates (m^3/day)

Four cases are addressed corresponding to four different units of measure for the animal dose D_A. In each case, the equivalent human dose is computed by normalizing the intake relative to body weight. For skin absorption, however, D_A refers not to an estimated intake, but simply to a concentration in water.

(i) D_A expressed in µg/day:

$$D_H\ (\mu g/day) = D_A \cdot \frac{W_H}{W_A}$$

(ii) D_A expressed as ppb in diet:

$$D_H\ (ppb) = D_A \cdot \frac{W_H}{W_A} \cdot \frac{I_A}{I_H}$$

$$D_H\ (\mu g/day) = D_A\ I_A \cdot \frac{W_H}{W_A}$$

(iii) D_A expressed as μg/l for skin contact:

$$D_H\ (\mu g/l) = D_A$$

$$D_H\ (\mu g/day) = 0.002\ D_A$$

(this assumes human absorption of 2 ml/day of water containing a pollutant)

(iv) D_A expressed as ng/m^3 for inhalation

$$D_H\ (ng/m^3) = D_A \cdot \frac{W_H}{W_A} \cdot \frac{R_A}{R_H}$$

$$D_H\ (\mu g/day) = D_A\ R_A \cdot \frac{W_H}{W_A} \cdot 10^{-3}$$

In order to facilitate the application of these formulae, the conversion chart in Table A-1 shows numerical conversion factors for experiments with mice and rats. The approach for converting acute doses is entirely analogous, except that the units of intake are μg rather than μg/day.

In the case of carcinogenic effects, it is sometimes assumed that equivalent doses are proportional to body area. The U.S. EPA recommends this method for designating equivalent doses of carcinogenic substances (U.S. EPA 1979). Presumably this method reflects a view that carcinogenesis is related to the area of some physiological membrane. It is also the logical choice when the route of exposure is skin absorption. Thus:

$$\frac{\text{Weight of substance to which human is exposed}}{\text{Body surface area of human}}$$

is equivalent to

$$\frac{\text{Weight of substance to which animal is exposed}}{\text{Body surface area of animal}}$$

Because the surface areas of similar solids are proportional to the squares of corresponding linear dimensions and volumes or weights are proportional to the cubes of corresponding linear dimensions, one can approximate surface area by weight raised to the two-thirds power. Thus

$$(\text{Body surface area}) \text{ is proportional to } (\text{Body Weight})^{2/3}$$

TABLE A-1. FACTORS FOR CONVERTING DOSES FROM LABORATORY ANIMAL STUDIES TO HUMAN EQUIVALENT DOSES

	ASSUMPTIONS[a]				HUMAN EQUIVALENT DOSE			
Species	Weight (kg)	Rate of Ingestion (kg/day)	Rate of Respiration (m^3/day)	Dose	μg/day Total	Food	μg/l Contact	ng/m^3 Breathing
Human	70	4	10.7					
Mouse	0.025	0.003	0.033	1 μg/day	2800			
				1 ppb	8.4	4.2		
				1 μg/l	0.002		1	
				1 ng/m^3	0.09			8.6
Rat	0.3	0.015	0.14	1 μg/day	233			
				1 ppb	3.5	1.75		
				1 μg/l	0.002		1	
				1 ng/m^3	0.03			3

---

[a] Equivalent human doses are assumed proportional to weight and rate of intake. Rates of respiration are based on minute volume while resting (Spector 1956).

Note: Adult mice and rats are usually heavier than 25 and 300 g. Thus the numbers above must be used with caution. If surface area is used as a normalizing factor rather than body weight, then human equivalent doses should be reduced by a factor of 14 for mice and a factor of 6 for rats.

This has the effect of reducing equivalent human doses by about 14 in the case of mice, and by about 6 in the case of rats (Table A-1).

In many experiments no explicit account is taken of time. However, time is an explicit variable in the multi-stage extrapolation described below, and it is an implicit variable in all other extrapolations. Cancer occurrence increases with age in both humans and experimental animals and is a multi-step, time-dependent process. For mice and rats the interval of the usual life span of 2-3 years is the normal exposure interval for a valid carcinogenicity study. The most plausible assumption is that the normal lifetime of an experimental animal is equivalent to the normal lifetime of a human.

Procedures for estimating human equivalent doses often account for time factors in several ways:

- If the substance was administered to experimental animals on an intermittent basis, e.g., 5 days per week, then the assumed dose is reduced by a corresponding factor, e.g., 5/7.
- If the duration of exposure was shorter than the experimental animal lifetime, then the assumed dose is reduced by the ratio of those times, i.e., duration/lifespan.

It should be noted that such procedures do not take into account the relevant pharmacokinetics, and are merely a device for reducing the dose and hence obtaining a more conservative risk estimate. They generally do not affect the results by more than a factor of 50%, which is small compared with the total range of uncertainty. Uncertainties due to dose estimation and techniques of extrapolation can often span several orders of magnitude.

A.3 ONE-HIT MODELS

The "one-hit" models describe a mechanism of carcinogenesis in which a single event triggers the cancer. The event may be a molecule of the carcinogenic substance reaching a suitable receptor site or it may be some more complex but undescribed happening. The basic supposition is that the probability of this event in a short time interval dt (short compared with the time of observation, which is usually the major part of a lifetime) is proportional to the duration of the time interval. The factor of proportionality, called the "hazard function," may be a function of time and of the dose level. Thus the hazard function is written $h(x,t)$ where x is the dose level and t is time, measured in lifetimes.

In the linear extrapolation, this function is taken to be proportional to dose:

$$h(x,t) = bx \qquad \text{(A-1)}$$

where b is a factor of proportionality and x is the dose level. The probability of a "hit," that is, initiation of cancer, is proportional to the duration of a time interval:

$$P\,\{\text{initiation of cancer in the interval } (t, t = dt)\} = bx\,dt$$

In this form one can see the reason for calling the extrapolation linear--doubling the dose, for example, doubles the probability of initiating cancer.

The multi-stage model generalizes this approach, replacing the product bx by the product of two polynomials, one a polynomial in t, the other a polynomial in x.

$$h(x,t) = \sum_{i=o}^{n} a_i t^i \sum_{j=o}^{m} b_j x^j \qquad \text{(A-2)}$$

This approach allows a great deal of flexibility, though as a practical matter the polynomials cannot be too large or one loses track of their significance.

Let Q(x,t) be the probability that no cancer has been initiated in the interval (0,t) when the animal has been subjected continually since time 0 to a dose level of x. The second underlying assumption is that the probability of initiating cancer at any particular time is independent of whether or not cancer has previously been initiated; this assumption allows us to multiply probabilities and

$$Q(x,t + dt) = Q\,(x,t)\,(1 - h(x,t)dt). \qquad \text{(A-3)}$$

Rearranging terms

$$\frac{\partial Q}{\partial t} + h(x,t)Q = 0$$

$$Q(x,t) = \exp\,[- \textstyle\int_o^t h(x,t)dt] \qquad \text{(A-4)}$$

Let P(x,t) be the probability that cancer is initiated in the interval (0,t)

$$P(x,t) = 1 - Q(x,t)$$
$$= 1 - \exp\left[-\int_0^t h(x,t)dt\right] \qquad \text{(A-5)}$$

P(x,t) can also be identified as the cumulative distribution function for the random variable "time until cancer is initiated"--that is, the probability that the time until cancer is initiated is less than t is P(x,t). The derivative dP/dt is the probability density function f(x,t) for these intervals

$$f(x,t) = \frac{dP}{dt}$$
$$= h(x,t) \exp\left[-\int_0^t h(x,t)dt\right]$$
$$= h(x,t)\, Q(x,t) \qquad \text{(A-6)}$$

The function f(x,t)dt has the interpretation of the probability that cancer is initiated in the interval (t,t+dt). Finally, we note that h(x,t)dt = f(x,t)dt/Q(x,t) can be interpreted as the probability that cancer is initiated in the interval (t,t+dt) given that it has not been initiated up until time t.

A.4 LINEAR EXTRAPOLATION

In the linear extrapolation h(x,t) is given by Equation (A-1).

$$Q(x,t) = e^{-bxt} \qquad \text{(A-7)}$$
$$P(x,t) = 1 - e^{-bxt} \qquad \text{(A-8)}$$

If there is a "background" or "spontaneous" cancer incidence present even when the dose rate of the toxic substance is zero, then one can use either of two smaller approaches. One can assume that h(x,t) has the form

$$h(x,t) = bx + c \qquad \text{(A-9)}$$

in which case

$$Q(x,t) = e^{-ct} e^{-bxt} \qquad \text{(A-10)}$$

$$P(x,t) = 1 - e^{-ct} e^{-bxt} \qquad \text{(A-11)}$$

At the conclusion of the experiment one can identify the fraction of animals in the control group which contracted cancer in spite of the fact they were not intentionally subjected to a carcinogen as the probability θ of "spontaneous" cancer. Then it is easy to see from Equations (A-10) and (A-11) that

$$Q(x,t) = (1 - \theta)e^{-bxt} \qquad \text{(A-12)}$$

$$P(x,t) = 1 - (1 - \theta)e^{-bxt} \qquad \text{(A-13)}$$

and hence

$$\theta = 1 - e^{-ct} \qquad \text{(A-14)}$$

Having measured θ by observing response in the control group, one could infer the value of c, but this is usually not done.

Alternatively, one can determine both parameters b and c by a data-fitting procedure involving the maximum likelihood estimators. This is the multi-stage procedure when two non-zero parameters in the polynomials are permitted. It is detailed below.

We have noted that P(x,t) is the cumulative distribution function for the random variable time-to-initiation-of-cancer. P(x,t) as a function of t has the form shown in Figure A-1.

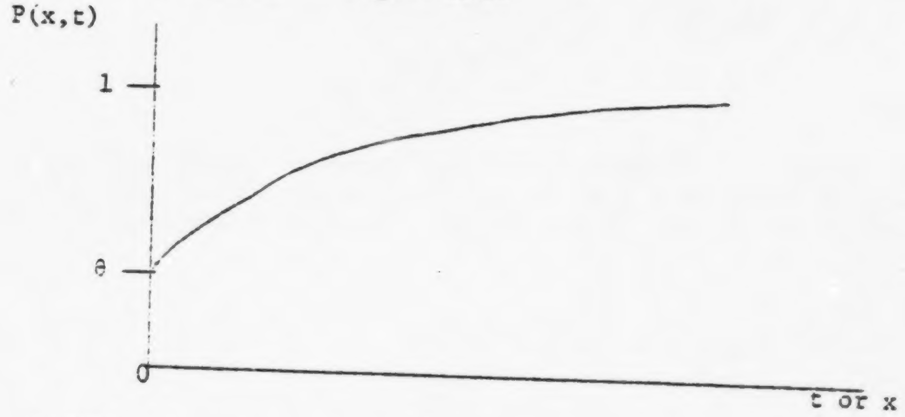

FIGURE A-1. CUMULATIVE DISTRIBUTION FUNCTION P(x,t)

Obviously, from Equation (A-13), $P(x,t)$ considered as a function of x has the same form as that when it is considered a function of t. For this reason it is common to regard $P(x,t)$ as the cumulative distribution function of a random variable called susceptibility. Thus, the fraction of experimental animals in whom cancer is initiated at dose x is regarded as a group of animals in whom tolerance is less than or equal to x. This logical transition from a determinate parameter of the experiment, the dose x, to a random variable, tolerance, is plausible but not necessarily correct. $P(x,t)$ is measured by giving a group of animals the dose x and noting the fraction in whom cancer is initiated. It is conceivable that $P(x,t)$ as a function of x could increase as the dose increases and then decrease if, for example, high doses brought into play a new mechanism, such as vomiting, not encountered at low doses. It is important to recognize that consideration of the dose-response curve as the cumulative distribution function of a random variable, tolerance, requires the supposition that $P(x,t)$ as a function of x increases monotonically.

The most rigorous mathematical procedure for estimating the parameters b and c (or b and θ) is maximum likelihood estimation. More commonly, experimenters simply plot the fractions of animals in which cancer is found at the conclusion of the experiment at time T and use these fractions as estimates of the parameter $P(x,t)$. In the linear extrapolation, it is customary to expand $P(x,T)$ about zero.

$$\begin{aligned} P(x,T) &\simeq 1 - (1 - \theta)(1 - bxT) \\ &\simeq \theta + bxT \end{aligned} \tag{A-14}$$

and to fit a straight line to the data points $P'(x_i,T) = P(x_i,T) - \theta = bx_iT$. Because the expansion in Equation (A-14) is valid only for small x, one should use data where x is as small as possible.

It should be noted that the crucial supposition in the linear model is the selection of the form for $h(x,t)$ given in Equation (A-1). The consequence of this selection is that the curve for $P(x,t)$ in the vicinity of $x = 0$ will have a positive slope. Because the data are gathered for relatively large values of x, the experiment does not test this supposition and therefore belief in the linear model amounts to an assumption. It is often argued that the real situation is unlikely to be worse than this and that therefore the linear model provides a conservative estimate of risk.

A.5 LOG-PROBIT EXTRAPOLATION

Log-probit extrapolation (also called Mantel-Bryan extrapolation after the original proponents of the method) assumes a different form for the dose-response curve. Specifically, it assumes that the logarithm of tolerance is normally distributed. There is little theoretical underpinning for this assumption, though a number of physiological variables (such as heights of humans) seem to follow this log-normal distribution.

The mathematical form of the dose-response curve is

$$P(x,T) = \int_{-\infty}^{a + b \log_{10} x} \frac{1}{\sqrt{2\Pi}} e^{-1/2\xi^2} d\xi \qquad \text{(A-15)}$$

On log-normal graph paper this function is a straight line with a slope of b probits (standard deviations) per decade of change in the dose x and a y-intercept of a probits, as shown in Figure (A-2).

The steeper (or the larger) the slope of this line the smaller the values of P(x,t) found by extrapolations to small values of x (large negative values of log x). One could plot the data and fit a straight line, either by eye or by some analytical procedure, thus finding values for the parameters a and b. However, the more common procedure is to set b = 1 and to find the best fit to the data of a line with this slope. It is argued that b = 1 is the shallowest slope observed over a wide variety of carcinogens already studied and that selecting a line with unit slope is therefore conservative.

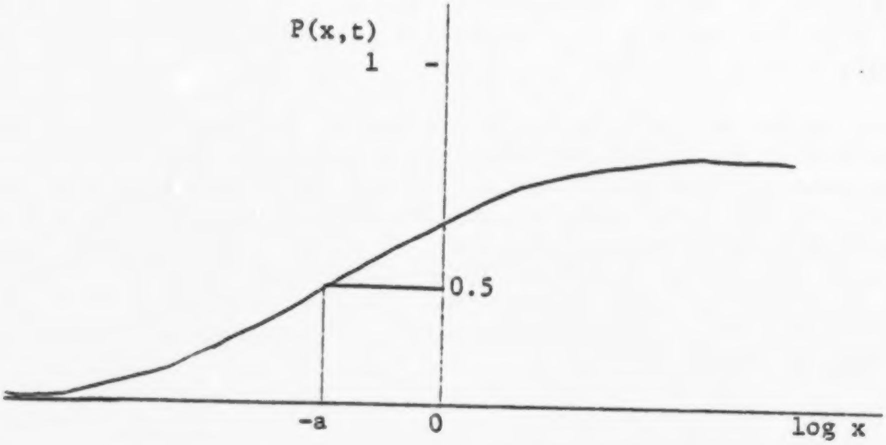

FIGURE A-2. LOG-PROBIT FORM FOR DOSE-RESPONSE CURVE

The supposition that the slope b = 1 is, of course, somewhat arbitrary but it is less significant than the equally arbitrary supposition that the dose-response curve should be described by Equation (A-15).

It can be seen that for large negative values of the variables of integration ξ the integrand in Equation (A-15) is very small. In fact, the function exp $(-\xi^2)$ and all its derivatives vanish as $\xi \rightarrow -\infty$. For this reason the log-probit extrapolation generally yields extremely low estimates of extrapolated risks at low dose levels. For the numbers actually encountered in experiments on one hand and in the environment, on the other, the difference between extrapolated risk by the log-probit method and the linear method can be several orders of magnitude. The log-probit extrapolation is therefore regarded as a probable low estimate of time risk, and the two methods are often taken as a way of bracketing the true risk. It is important to recognize that both methods produce results strongly dependent on the presumed form of the dose-response curve.

It should also be noted that this method can deal only with the difference between response at a dose x and response when x = 0 (the "spontaneous" rate), since log 0 = $-\infty$. Thus, there is no possibility of fitting a line or a curve through the datum when x = 0.

Multi-Stage Extrapolation

The Hartley-Sielken extrapolation is a one-hit model in which more flexibility is allowed in the form of the hazard function h(x,t). It thus entails fewer presuppositions about the dose-response curve. In addition the method follows a more rigorous mathematical procedure for estimating the value of the unknown parameters, and it takes explicit account of the time-to-initiation-of-cancer whenever these data are recorded.

In order to avoid confusing generality we shall adopt a specific form for the hazard function which is not too complicated and yet provides sufficient flexibility for purposes of risk estimates, namely

$$h(x,t) = ax^2 + bx + c \qquad \text{(A-16)}$$

where a, b, and c are parameters to be found from the data. Recalling equation (A-5) we see that

$$P(x,t) = 1 - \exp\,[-(ax^2 + bx + c)t] \qquad \text{(A-17)}$$

will be the form of the dose-response curve at any time. We note that if c ≠ 0 there is a "spontaneous" incidence of cancer; if b ≠ 0, the extrapolation to low doses is linear; by including the term ax^2 we allow for the possibility that response at low doses may not be linear, in which case we would expect to find $a \neq 0$, $b = 0$.

Most available data record only the number of animals which had cancer at the conclusion of the experiment. For such experiments we have a sample of $P(x,T)$ for various values of x. Sometimes the number of animals with cancer at some intermediate time is reported in which case we have samples of $P(x,T_i)$ for other values of T and various values of x. Occasionally when the cancer can be detected without killing the animal (as in the case of skin cancers) one has the time-to-initiation-of-cancer as well as dose for each animal. The multi-stage method accommodates all these possibilities and produces the values of a, b, and c which best fit the totality of the data.

Since none of the data available in these studies records time-to-time initiation-of-cancer for each animal, we shall not carry the terms necessary to accommodate these data in the mathematical development which follows. The likelihood function L is the product of terms of the form $P(x,t)$ given by Equation (A-17) and its complement $Q(x,t) = 1 - P(x,t)$.

$$L = \prod_{i=1}^{N} P(x_i,t_i)^{n_i} \, Q(x_i,t_i)^{N_i - n_i} \qquad \text{(A-18)}$$

where i is the index for the N experimental data points, each of which has a value for x_i and t_i associated with it; and n_i is the number of positive responses, N_i is the total number of animals and $N_i - n_i$ is the number of negative responses

$$\log L = \sum_{i=1}^{N} n_i \, P(x_i,t_i) + (N_i - n_i) \, Q(x_i,t_i) \qquad \text{(A-19)}$$

The standard procedure is to differentiate Equation (A-19) with respect to the unknown parameters and to set the derivatives equal to zero in order to find the maximum of log L. However, it is more convenient simply to seek the maximum of log L by a hill-climbing method. One selects initial values of a, b, and c, and then evaluates log L with small changes, first of a, then of b, then of c, then of a again, etc., continuing this procedure until log L begins to decrease. In this way one can find the values of a, b, and c that maximize log L or L. These are the maximum likelihood estimators.

If it should turn out that $a = 0$, then the result obtained is equivalent to the linear extrapolation found earlier. In the former case, however, we imposed the form from the beginning; here we have allowed the data to produce the form. Note, too, that this method automatically introduces variations in the duration of an experiment, and that it automatically weights data where many animals are involved more heavily than data where only a few are involved. For these reasons, the multi-stage method seems superior to either the linear extrapolation or the log-probit extrapolation.

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